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# BRITISH JOURNAL OF PREVENTIVE & SOCIAL MEDICINE

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## CONTENTS

PAGE

**Blood Groups and Susceptibility to Disease.** J. A. Fraser Roberts .. .. .. .. 107

**The Nature of the Determinants of Rhesus Isoimmunization.** George Knox and William Walker .. .. .. .. .. .. .. .. .. .. .. 126

**Some Aspects of Growth with Norms from Birth to 18 Years.** W. H. Hammond .. .. 131

**An Examination of the Association between Housing Conditions and Pulmonary Tuberculosis in Glasgow.** J. S. McMillan .. .. .. .. .. .. .. .. 142

**Observations on Routine Medical Examinations of University Entrants in Northern Ireland.** W. Johnston, E. A. Cheeseman, and J. D. Merrett .. .. .. .. .. 152

**A Note on the Association between Smoking and Disease in Men in the Seventh Decade.** R. G. Brown, Thomas McKeown, and A. G. W. Whitfield .. .. .. .. 162

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# BLOOD GROUPS AND SUSCEPTIBILITY TO DISEASE: A REVIEW

BY

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## (1) Introduction and Historical Survey

When the Rhesus blood-group system was discovered it was almost immediately established that maternal-foetal incompatibility was the cause of haemolytic disease of the foetus and the newborn. There has also been much work on maternal-foetal incompatibility in relation to possible differential elimination at a very early stage of life. These important subjects are not dealt with in this paper, which is concerned with another question, which, though it was posed earlier, has only received a clear positive answer during the past few years. This is whether persons belonging to different blood groups may differ in their susceptibility to certain diseases.

In the early days of work on the ABO system it was natural to ask two questions: first, whether the frequencies of the groups are different in people belonging to different races; and secondly, whether the frequencies of the groups are different in persons suffering from different diseases. Both questions were asked, and at about the same time, but the fate of the two lines of inquiry was strangely different. In 1919 Hirschfeld and Hirschfeld published their classical paper. Making use of the special opportunity offered by the very varied racial composition of the Allied army in Macedonia, they selected 8,000 soldiers belonging to sixteen ethnic groups and showed conclusively that there were indeed large differences in blood-group frequencies. Their paper, in fact, foreshadowed in broad outline the pattern which has become steadily more detailed from that time to the present day. The first important paper on blood groups and disease was that of Buchanan and Higley (1921). Their plan was the same as that of the Hirschfelds; they examined at the Mayo Clinic the blood-group frequencies of some 2,400 patients suffering from a variety of diseases. The discovery that in all probability there were differences in their material was only narrowly missed. During subsequent years a large literature accumulated, but it would probably be true to say that during nearly 30 years only one positive association emerged, and that not very clearly, for the numbers were relatively small and the result was obscured in the growing volume of negative and conflicting findings. It is instructive to look back in the light of our present knowledge and to consider what the difficulties were that delayed for 30 years the discovery of associations that now seem so obvious and for which overwhelming evidence had rapidly been forthcoming.

The principal difficulties may be listed as follows:

(*A*) *Numbers*

Even when an association is relatively large, the numbers needed for establishing it are to be counted in thousands rather than in hundreds, and rarely indeed were anything like the necessary numbers forthcoming. Furthermore, a lack of appreciation of the limitations of small series and what they can reveal served to complicate and confuse the literature. Unless and until it is known that there is something definite to look for it is expensive and difficult to carry out *ad hoc* inquiries. With anthropological investigations, normal blood donors have been counted in millions and have provided ready-made data. It is only within the last 8 or 10 years that routine blood-grouping has become general for hospital patients suffering from certain diseases during the course of which a transfusion will probably or possibly be needed. We now have the advantage of being able to analyse existing hospital records, though at most hospitals this will only apply to a few diseases. Most series counted before 1953 were small and could yield results only if combined with others. This leads us to the difficulties described under (*B*) and (*C*).

(*B*) *Reliable and Comparable Techniques*

Much of the earlier grouping was reasonably reliable and consistent, but this was not universally true. Until more recent times, most workers would have rightly thought it dangerous to add together and compare frequencies obtained by different workers at different centres. If this is to be done the figures must be reliable within a small margin, which is generally true to-day for the ABO system. With Rhesus, however, the position is still rather like it used to be with ABO. There appear to be discrepancies between centres which make special precautions necessary if fine comparisons are attempted between series obtained from different laboratories. We have to recall, therefore, that the earlier investigators were faced with problems which with ABO do not now trouble us seriously.

(*C*) *Controls*

To-day, in many countries, reliable figures for blood-group frequencies are available for the general population. These are based on counts of blood-donors or on unselected series of pregnant women. Within single countries and sometimes over quite short distances, there may be apppreciable differences in blood-group frequencies. These are constantly being more efficiently mapped, and control data of increasing value are becoming available to those who would study disease associations. This advantage was largely denied to the earlier workers, who, as will be mentioned later, were often in difficulty over the selection of suitable control series against which to match their patients. It added greatly to the laboriousness of the task if the investigator had to group his own controls. On the other hand, if figures for different diseases were compared, other difficulties obviously arose.

(*D*) *Classification of Diseases*

In searching for blood-group associations races classify themselves, but it is by no means so obvious what groupings of disease entities should be made. Fine subdivisions mean smaller numbers, and it was very natural to look at, say, carcinoma taken as a whole. It is only in the light of after knowledge that we can see that the broad groupings often selected in the past were not happily chosen and could not have revealed anything.

(*E*) *Statistical Methods*

Hirschfeld and Hirschfeld (1919) did not use any special statistical techniques, nor were these needed for the establishment of the racial differences they found to exist; the figures were large enough to speak for themselves. If Buchanan and Higley (1921) had counted twice the number they did count, they would probably have discovered one association, and perhaps two. If they had counted three times as many, they would certainly have done so, and without the use of any statistics other than the calculation of percentage group frequencies. Statistical techniques do, of course, improve the analysis; more is extracted from the data. Sometimes, however, a discovery may be made by their use that would otherwise be missed. This happened with Buchanan and Higley, for a simple analysis would have shown that the group frequencies for the different diseases were suspiciously heterogeneous, and that there was at least a problem for further investigation. To-day, the use of efficient statistical techniques is so universal that it is unlikely that much will be missed through their neglect.

In spite of the difficulties, the discovery that there were associations between blood groups and particular diseases might well have been made by Buchanan and Higley. They did not fail by very much where, working on similar lines, the Hirschfelds had succeeded. Apart from the interest of contemplating the years that the locust has eaten, and of reflecting on the possible consequences had the discovery of associations been firmly established 30 years earlier than it was, a closer examination of their data is of value from the point of view of the planning of future work, and not only in this particular field.

Buchanan and Higley were stimulated to make their count by a paper published by Alexander (1921), one of the first, or perhaps the first, in this field. Alexander gave the following frequencies for fifty patients suffering from various forms of carcinoma: O, 14; A, 14; B, 16; AB, 6. He contrasted these with 175 results from fifty normal subjects, fifty suffering from tuberculosis, fifty with syphilis, and 25 with tetanus, the totals being: O, 84; A, 62; B, 22; AB, 7. Alexander concluded that persons of Groups B and AB were especially susceptible to carcinoma. Stimulated by this paper, Buchanan and Higley analysed the results for 2,446 patients grouped at the Mayo Clinic from

January 1917 to May 1921. They classified the patients into seventeen diseases or groups of diseases, with a residual miscellaneous group. A summary of the figures is presented in Table I (combining the three small series of leukaemias), together with a test for homogeneity in regard to Groups O and A.

TABLE I

DATA OF BUCHANAN AND HIGLEY (1921)

| | Disease | O | A | B | AB | Total | O, A |
|---|---|---|---|---|---|---|---|
| 1 | Carcinoma .. | 140 | 119 | 22 | 11 | 292 | 0·01 |
| 2 | Pernicious Anaemia.. | 189 | 202 | 46 | 20 | 457 | 4·53 |
| 3 | Leukaemia .. | 35 | 22 | 16 | 1 | 74 | 1·36 |
| 4 | Splenic Anaemia | 23 | 17 | 1 | — | 41 | 0·23 |
| 5 | Haemophilia and Purpura | 19 | 16 | 4 | 1 | 40 | 0·01 |
| 6 | Acute and Chronic Kidney Disease .. | 37 | 21 | 4 | — | 62 | 2·38 |
| 7 | Cardiac, Valvular, and Myocardial Disease | 10 | 7 | 3 | — | 20 | 0·18 |
| 8 | Diseases of the Thyroid .. | 23 | 12 | 2 | — | 37 | 2·03 |
| 9 | Tumours other than Cancer .. | 33 | 21 | 10 | 1 | 65 | 1·19 |
| 10 | Calculi (Nearly All Cholelithiasis) .. .. | 63 | 55 | 12 | 4 | 134 | 0·00 |
| 11 | Fibroid Uterus | 54 | 64 | 13 | 6 | 137 | 2·99 |
| 12 | Secondary Anaemia (All Causes) .. | 82 | 82 | 21 | 9 | 194 | 0·90 |
| 13 | Acute and Chronic Gallbladder Disease | 95 | 62 | 13 | 6 | 176 | 2·93 |
| 14 | Chronic Ulcers (Nearly All Peptic) .. | 102 | 55 | 8 | 7 | 172 | 8·02 |
| 15 | Jaundice (All Causes) .. | 64 | 83 | 20 | 6 | 173 | 6·11 |
| 16 | Miscellaneous | 177 | 150 | 26 | 19 | 372 | 0·02 |
| Total .. .. .. | | 1,146 | 988 | 221 | 91 | 2,446 | |
| Per cent. Frequencies | | 46·85 | 40·39 | 9·04 | 3·72 | | |
| Degrees of Freedom 15; $P=0·005$ .. | | | | | | $\chi^2 = 32·89$ | |

Looking at the percentage frequencies for the larger groups, Buchanan and Higley came to the following conclusions:

"(1) There is no relationship between blood groups and malignancy as suggested by Alexander.

(2) There is no relationship between blood groups and any disease in which sufficient data are available to justify a conclusion.

(3) The percentages originally presented by Moss are approximate and capable of considerable variation, without special significance.

(4) Nationality should be taken into consideration in the presentation of statistical studies of blood-grouping."

Applying a test for homogeneity, however, as shown in Table I, it can be seen that the material is suspiciously heterogeneous. If indeed there are no associations, the probability of getting such a divergence by chance is about 1 in 200. It can be further seen that this is nearly all due to three disease groups, namely, chronic ulcers, jaundice, and pernicious anaemia. Two of these divergencies we now know to be real.

Internal evidence suggests that the technique of grouping was very good. The overall percentage frequencies would do very well for the frequencies now well established in those parts of the United States. Fisher's test for reasonableness of group proportions (Dobson and Ikin, 1946) yields a non-significant $\chi^2$.

Buchanan and Higley did not have the advantage of outside controls for comparison, and they had been struck by the discrepancies in the series so far published. They were thus confined to comparisons within the material, but, as has just been mentioned, these could have led them, if only tentatively, to the right conclusion. There was a special difficulty, however. They were also very conscious of the big racial differences recently demonstrated by the Hirschfelds. They showed patients of different origins separately, and indeed, if those not native to the United States are omitted (and it is difficult to see what else they could have done), the evidence for heterogeneity is considerably weakened. Nevertheless, it is a pity that after looking at the figures they did not conclude that Group O was in excess with ulcers and Group A with jaundice and pernicious anaemia. Had they done so, others would probably at once have made further studies on these particular diseases and two associations would then have been discovered.

The subsequent literature is voluminous and for the most part unrevealing. In many studies the numbers were far too small. Where they were fairly large the disease groups chosen (as we know now, though it could not have been known then) were too broad, for example, carcinoma, or mental diseases. Furthermore, the inquiries tended to be diverted by the idea that diseases could change the blood group, a conception which was not finally disposed of until the mid-1930s. In fact the next positive indication of any weight did not appear till 1936, when Ugelli discovered, or re-discovered, the association between Group O and gastroduodenal ulcer.

Ugelli (1936) chose peptic ulceration for a special reason. Impressed by the known anthropological associations, he felt that studies should be made on blood-group frequencies in relation to constitutional type; and so he chose peptic ulcer as a disease in which it was strongly suspected that psychoconstitutional factors are important. His series showed: Group O, 127; Group A, 81; Group B, 29; Group AB, 7. The percentage frequencies are respectively: 52·0; 33·2; 11·9; 2·9. He quoted five series of Italian frequencies. Unfortunately they showed wide discrepancies. He preferred the series of Viola (1934), both on account of its relatively large numbers and because it corresponded well with a small series of his own, based on healthy subjects. Actually, Viola's sample seems rather high in A and low in O. In any event, Ugelli came to the correct conclusion; he stated in his summary that there was an excess of Group O.

In 1949, Lessa and Alarcao published a valuable review of the literature, but the only indication of an association which could be regarded as reasonably probable was peptic ulcer, as previously indicated by the results of Buchanan and Higley and of Ugelli. Their own series of some 500 confirmed the excess of O. By this time, however, so much had been written, there had been so much discussion about non-significant differences, so much was negative, and so many conflicting views had been expressed, that Ugelli's undoubted discovery, supported by this later result, seems to have been generally overlooked. Something more was needed, a result based on really large numbers, a significance so overwhelming that it could not be ignored, before it was likely to be generally realized that there are indeed large and important associations between blood groups and some common chronic diseases of adult life. Before proceeding with the story, however, one striking and so far isolated result must be mentioned.

In 1951 new ground was explored by Struthers. He examined the ABO groups in 400 consecutive infants coming to *post-mortem* examination at a children's hospital in Glasgow. He found an excess of children of Group A. Further analysis showed that the excess was due to those exhibiting bronchopneumonia. This work is mentioned more fully in a later section.

The long-postponed general realization that there are indeed large and important associations between ABO blood groups and disease came in 1953. It was due to the initiative and persistence of Professor Ian Aird. Like Ugelli, Aird selected one particular disease, namely cancer of the stomach, and again, like Ugelli, had a particular reason for doing so. The incidence of cancer of the stomach shows very large differences in different parts of the British Isles. In particular, this disease is about twice as frequent in the north of England as in the south. Could some racial or constitutional factor be responsible? If so, it would be a good plan to look at ABO blood group frequencies, which also show considerable and regular differences in the British Isles. Aird was determined to collect large numbers, and thanks to the growing practice of routine blood-grouping of patients, was able to do so from the existing records of a large number of hospitals. The hypothesis proved irrelevant, as in fact the association was with Group A, which is commoner in the south of England, where cancer of the stomach is less common. But that did not matter, for what emerged was that patients with cancer of the stomach have a higher frequency of Group A than do corresponding controls. On a total of some 3,500, the result was overwhelmingly significant. A series contributed by Dr. L. P. Holländer of Basel showed the same excess of Group A. The results were published by Aird, Bentall, and Roberts (1953).

Stimulated by this positive finding, these workers carried out a further study of those diseases in which routine hospital groupings are commonly made (Aird, Bentall, Mehigan, and Roberts, 1954). The association between Group O and peptic ulcer was rediscovered, and this time at three separate centres and on numbers large enough to dispel any doubt. Three cancers, those of the colon and rectum, lung, and breast, gave negative results.

During the short time that has since elapsed, much progress has been made, and results have been published from a number of different countries. There is now strong evidence that the association between Group O and duodenal ulcer is closer than that between Group O and gastric ulcer, a finding that the figures of Aird and others (1954) were insufficient to establish. Pernicious anaemia shows an association with Group A. There is fairly strong evidence for a similar association in diabetes mellitus. It has also been discovered, by Clarke, Edwards, Haddock, Howel-Evans, McConnell, and Sheppard (1956), that duodenal ulcer is commoner in non-secretors of substances with ABO specificity than it is in secretors. A considerable body of data has been collected on Rhesus, though so far this is almost entirely confined to the simple categories positive and negative. With the subdivisions of Group A and with some of the other blood-group systems a beginning has been made, but numbers are as yet much too small for any conclusions to

emerge. Most of this paper presents an analysis of the evidence, under the heading of each separate disease, for the ABO system. As a preliminary, however, it is necessary to say a word about the methods of calculation used.

### (2) Methods of Calculation

Nothing need be said about the use of standard statistical procedures, but there is one special problem of great importance in this work which requires a short description, as the methods for dealing with it are fundamental to the analyses made in this paper. It is essential to combine data from different countries, and different centres within countries, all with different group frequencies in their populations. In the first place, the numbers available at any one centre must often be individually too small, and so they have to be combined with others. In the second place, it is necessary to arrive at a combined weighted estimate of the strength of an association, pooling all available data, and then to test its significance. Thirdly, it is necessary to see whether the different centres are or are not homogeneous in respect of the existence and of the magnitude of an association. In general, simple addition of the frequencies will not yield a correct combined estimate, or lead to valid tests of significance. To take an unweighted average of the differences or incidences, as between disease and control series at the different centres, is inefficient, as it does not allow for differences in the accuracy with which these proportions have been determined. What is required is to give the difference in proportion, or in relative incidence, for each area a weight which is inversely proportional to its estimated variance.

The method originally described by Aird and others (1954) is due to R. A. Fisher and was used for analysis of the somewhat similar problem of possible associations between blood groups and sex (Fisher and Roberts, 1943). Although the second method, which is described below, is the one employed in this paper, the first is also given because it has been used in a number of other papers.

Let us take as an illustration the comparison of Group O and Group A in a disease series and in the corresponding controls. In each area let $n_1$ be the number of Os and As in the disease series, giving a proportion of A/(A + O) of $p_1$;

$n_2$ and $p_2$ are the corresponding figures for the controls;

$p_1 + q_1 = 1$, and $p_2 + q_2 = 1$;

$p_1 - p_2 = d$;

$$w = 1/\left(\frac{p_1q_1}{n_1} + \frac{p_2q_2}{n_2}\right);$$

the combined weighted mean difference for all areas $= Swd/Sw$;

$\chi^2$ for the difference, with one degree of freedom $= (Swd)^2/Sw$;

$\chi^2$ for the homogeneity of areas $= Swd^2 - (Swd)^2/Sw$, with degrees of freedom one less than the number of areas.

The second method is that of Woolf (1955). It is very similar in principle, but starts with relative incidences instead of differences. In each area let the number of Os and As in the disease series be $h$ and $k$, and in the corresponding control series $H$ and $K$, then the incidence of the disease in persons of Group O is $hK/Hk$ compared to 1 in persons of Group A.

$x = hK/Hk$;

$y = \log_e x$;

$$w = 1/\left(\frac{1}{h} + \frac{1}{k} + \frac{1}{H} + \frac{1}{K}\right);$$

$Y = Swy/Sw$;

$\chi^2$ for the difference from unity, with one degree of freedom $= (Swy)^2/Sw$;

$\chi^2$ for the homogeneity of areas $= Swy^2 - (Swy)^2/Sw$, with degrees of freedom one less than the number of areas;

estimated mean relative incidence = antilog $Y = X$;

standard deviation of $Y = 1/\sqrt{(Sw)}$;

approximate 95 per cent. fiducial limits $= Y \pm 1{\cdot}96$ S.D.;

antilogs give fiducial limits of $X$.

Woolf's method has the advantage that the results come out in a form with a simple and direct physical meaning; it is natural to think of diseases in terms of incidence. For example, we can say that the relative incidence of duodenal ulcer is 1·38 in persons of Group O as compared with 1 in persons of the other groups. The second advantage is that Woolf's method can be used for combining and comparing populations with widely differing blood-group frequencies. When, however, the populations considered do not show any wide divergences, for example, throughout Western Europe, the two methods give closely similar results.

### (3) Duodenal Ulcer

Relatively large series have now been published for London, Manchester, Newcastle-upon -Tyne, Liverpool, Glasgow, Copenhagen, Oslo, Vienna, and Iowa. Table II gives a brief summary of the findings. These figures cannot be used for statistical tests, but they do bring out some of the essential features of the association.

TABLE II

DUODENAL ULCER

Brief Summary of results from Nine Centres shown separately in Table III

| Blood Group | Duodenal Ulcer | | Controls* Percentages | Per cent. Increase or Decrease on Controls |
|---|---|---|---|---|
| | Numbers | Percentages | | |
| O | 4,424 | 53·48 | 45·78 | +16·8 |
| A | 2,902 | 35·08 | 40·43 | −13·2 |
| B | 694 | 8·39 | 10·13 | −17·2 |
| AB | 252 | 3·05 | 3·66 | −16·7 |
| Total | 8,272 | | | |

Approximate Relative Incidences:

O : A, 1·35; O : B, 1·41; O : AB, 1·40;
O : (A+B+AB), 1·36; A : B, 1·05; A : AB, 1·04;
AB : B, 1·01.

* Controls weighted according to number of patients with duodenal ulcer at each centre.

In duodenal ulceration, the proportion of Group O is substantially increased, all the other groups being correspondingly diminished, and to much the same extent. Actually, the approximate relative incidences, simply calculated from the percentage group frequencies, are very similar to the values accurately calculated, as shown in Table III. It will be seen that the incidence of the disease in persons of Groups A, B, and AB is closely similar, the whole difference being between Group O and the remainder.

Table III gives an analysis of the results from the various centres. It will be seen that the higher incidence in Group O as against both Group A and Group B is enormously significant; even Group AB, with its relatively small numbers, differs highly significantly from Group O.

It will be noted, however, that the areas show significant heterogeneity. Each one separately shows the increased incidence in Group O, the $\chi^2$'s being over 20 at each of six of the areas taken separately. The heterogeneity is due to lower figures at Manchester, Glasgow, and Vienna, though the Manchester series is rather small.

TABLE III

DUODENAL ULCER

Analysis of Incidence of Disease in Persons of Group O Relative to its Incidence in Persons of the Other Groups

| | Centre† | No. in Disease Series | Relative Incidence O : A | $\chi^2$ | Relative Incidence O : B | $\chi^2$ | Relative Incidence O : AB | $\chi^2$ | Relative Incidence O : (A+B+AB) | $\chi^2$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | London | 946 | 1·59 | 38·33 | 1·41 | 6·93 | 1·41 | 2·66 | 1·54 | 39·83 |
| 2 | Manchester | 423 | 1·27 | 4·77 | 1·06 | 0·09 | * | * | 1·21 | 3·76 |
| 3 | Newcastle | 482 | 1·46 | 14·20 | 1·92 | 11·32 | * | * | 1·57 | 22·75 |
| 4 | Liverpool | 1,059 | 1·64 | 47·89 | 1·41 | 8·53 | 0·92 | 0·20 | 1·54 | 44·26 |
| 5 | Glasgow | 1,642 | 1·10 | 2·32 | 1·31 | 7·39 | 1·61 | 6·05 | 1·17 | 7·51 |
| 6 | Copenhagen | 680 | 1·42 | 17·50 | 1·53 | 8·84 | 2·23 | 10·16 | 1·48 | 25·06 |
| 7 | Oslo | 579 | 1·49 | 19·78 | 2·03 | 13·39 | 1·76 | 4·83 | 1·56 | 26·77 |
| 8 | Vienna | 1,160 | 1·21 | 7·76 | 1·35 | 8·51 | 1·06 | 0·17 | 1·22 | 9·95 |
| 9 | Iowa | 1,301 | 1·34 | 20·26 | 1·35 | 6·71 | 1·88 | 9·81 | 1·37 | 26·49 |
| 10 | Boston | 144 | — | — | — | — | — | — | 1·86 | 13·16 |
| Total | | 8,416 | | | | | | | | |
| Mean Weighted Relative Incidence | | | 1·36 | | 1·41 | | 1·35 | | 1·38 | |
| | Total | | | 172·82 | | 71·71 | | 33·88 | | 219·53 |
| | Difference from Unity, D. of F. = 1 | | | 144·53 | | 61·93 | | 17·38 | | 192·06 |
| $\chi^2$ | Heterogeneity, D. of F. = 9 | | | | | | | | | 27·48 |
| | Heterogeneity, D. of F. = 8 | | | 28·28 | | 9·78 | | | | |
| | Heterogeneity, D. of F. = 6 | | | | | | | 16·50 | | |
| *P* | Heterogeneity | | | ·004 | | ·3 | | ·01 | | ·001 |

* Numbers too small.

†(1–3) Aird, Bentall, Mehigan, and Roberts (1954);
(4) Clarke, Cowan, Edwards, Howel-Evans, McConnell, Woodrow, and Sheppard (1955);
(5) Brown, Melrose, and Wallace, (1956);
(6) Køster, Sindrup, and Seele (1955);
(7) Heistø (1956);
(8) Speiser (1956);
(9) Buckwalter, Wohlwend, Colter, Tidrick, and Knowler (1956 b).
(10) Mayr, Diamond, Levine, and Mayr (1956).

To the results of Table III may be added the findings from three other centres. The figures for Italy (Ugelli, 1936) have been quoted, and also those of Lessa and Alarcao (1949) from Portugal. They are not included in the Tables because gastric and duodenal ulcers are treated together, and with Ugelli's series it is difficult to choose a suitable control series. The third country is Australia, where, at Sydney, Billington (1956b) finds a very high excess of Group O in a relatively small series. His further findings are, however, so remarkable that his series has not been included in the foregoing comparisons. There is also a small series from Boston in a paper by Mayr, Diamond, Levine, and Mayr (1956) which is mentioned later. They simply give the number of Os and the total number for duodenal ulcer; small though the series is, the excess of Group O is highly significant.

It may be concluded, therefore, that, in all the countries where studies have so far been carried out, duodenal ulcer is considerably more common in persons of Group O than in persons belonging to the other groups, and that there are good indications that differences between the other three groups are small or non-existent. But, though the excess in persons of Group O appears in all series, it is significantly variable in amount, Glasgow and Vienna showing lower figures than other centres. There seems to be no obvious reason for this variation; as regards population blood-group frequencies at least, these two cities are at opposite ends of the scale in the material so far published. It is not surprising perhaps that when numbers become sufficiently large differences should be revealed; no doubt they will in time furnish valuable clues to the meaning of the associations.

The search for differences when subdivisions are made is of great potential value. But of course with subdivision the numbers become progressively smaller and truly vast series are required. Some of the authors quoted have looked at sex and age differences in considerable detail, but so far there is nothing substantial to contradict the hypothesis that the difference between persons of Group O and the other groups is true of both sexes and over all ages.

Attempts have been made to look for differences in relation to the severity of the disease, notably by Buckwalter, Wohlwend, Colter, Tidrick, and Knowler (1956b) and Brown, Melrose, and Wallace (1956) but with two possible exceptions nothing has yet emerged. Thus, Brown and others (1956) found no appreciable difference between those having bleeding or perforated ulcers and the remainder. Nor was there any difference between those macroscopically diagnosed, that is, largely surgical cases, and those radiologically diagnosed, who included many medically treated cases. At Liverpool, Clarke, Cowan, Edwards, Howel-Evans, McConnell, Woodrow, and Sheppard (1955) actually found a greater excess of Group O in those radiologically diagnosed. Buckwalter and others found no difference between medically and surgically treated cases. Køster, Sindrup, and Seele (1955) suggested that the blood group association in peptic ulcer and in cancer of the stomach might be related to level of output of hydrochloric acid. But Buckwalter and others found no difference between those respectively high and low in free hydrochloric acid.

One of the exceptions mentioned above is of much potential interest, should it be confirmed on larger numbers. Brown and others (1956) noted that the excess of O was particularly high in those suffering from anastomotic or stomal ulcer, which may be regarded as the most extreme form of the ulcer diathesis. A re-examination of the data of Aird and others (1954) lends some corroboration. The results are shown in Table IV.

TABLE IV

COMPARISON OF STOMAL ULCER WITH DUODENAL ULCER

| | Centre* | Stomal Ulcer | | Duodenal Ulcer | | Relative Incidence Stomal *v.* Duodenal O : (A+B+AB) | $\chi^2$ |
|---|---|---|---|---|---|---|---|
| | | O | A+B+AB | O | A+B+AB | | |
| 1 | Glasgow | 55 | 24 | 947 | 695 | 1·68 | 4·34 |
| 2 | London | 35 | 18 | 506 | 394 | 1·51 | 1·94 |
| 3 | Newcastle | 16 | 11 | 281 | 186 | 0·96 | 0·01 |
| Total | | 106 | 53 | 1,734 | 1,275 | | 6·29 |
| Mean Weighted Relative Incidence | | | | | | 1·46 | |
| $\chi^2$ | Difference from Unity, D. of F. = 1 | | | | | | 4·88 |
| | Heterogeneity, D. of F. = 2 | | | | | | 1·41 |
| *P* | Heterogeneity | | | | | | 0·5 |

*(1) Brown, Melrose, and Wallace (1956); (2–3) From data of Aird, Bentall, Mehigan, and Roberts (1954).

The relative incidence of stomal ulcer in persons of Group O is about double the figure for persons of the other groups. The most useful comparison, however, is with those suffering from duodenal ulcer at the same centres. Measuring the relative incidence against the already high figure shown by patients with duodenal ulcer, the incidence in Group O is further raised by an indicated figure of 1·47. The $\chi^2$ for the difference even on these small numbers is 4·88 for one degree of freedom and so is significant at the 5 per cent. level. Of course, it would be unwise to accept this result as more than a suggestive indication, and it is to be hoped that further results will soon be forthcoming.

The other exception was noted by Buckwalter and others (1956b). Those whose free hydrochloric acid was increased after histamine were higher in Group O than those in whom no increase was produced. Comparing Groups O and A, $\chi^2$ was 4·44 for one degree of freedom and so significant at the 5 per cent. level. This finding also is an indication for further work.

A major discovery, already briefly mentioned, has been made by Clarke and others (1956). As is well known, some persons secrete in their body-fluids substances having ABO specificity, whereas others do not. It is a simply inherited difference, secretion being dominant to non-secretion. The saliva of a secretor of Group A contains group-specific substance A; a secretor of Group B, substance B; a secretor of Group AB, both substances. A secretor of Group O secretes H substance, which is not group-specific, being secreted by secretors of the other groups also. The H substance in the saliva of persons of Group O was detected by using extracts of Ulex, a technique which has proved very reliable. In brief summary, 514 patients with duodenal ulcer included 180 non-secretors (35·0 per cent.), while 491 controls included 119 (24·2 per cent.), a figure close to that accepted as the usual frequency of non-secretors in Great Britain. There was no significant difference as between the sexes, nor as between persons of the different groups, including Group O. The overall difference between ulcer patients and controls gave a $\chi^2$ of 13·97 for one degree of freedom, and so is very highly significant.

To sum up, there is overwhelming evidence that duodenal ulcer is commoner in persons of Group O than in those belonging to the other groups. Differences as between the other groups are very small and are non-significant. The overall incidence in persons of Group O is 1·38 compared to 1 in those belonging to the other groups, this result being based on more than 8,000 cases collected at a number of centres in various different countries. While, however, the excess is found at all centres so far studied, there is significant variation in the level of the excess as between the different centres. Subdivision of the material by sex, age, severity, etc. has not so far shown any differences, except for two possibly suggestive findings on which there is some evidence: that the excess of Group O is particularly marked in those with stomal or anastomotic ulcers; and that the excess is higher in those who respond to histamine by a rise in free hydrochloric acid. There is extremely strong evidence that duodenal ulcer is commoner in those who do not secrete the ABO substances in their body-fluids.

### (4) Gastric Ulcer

In the earlier studies, gastric and duodenal ulceration were considered together. In the series of Aird and others (1954) patients with gastric ulcer differed with high significance from the controls. The excess of Group O was lower than in duodenal ulcer, but the difference was not significant. With the appearance of further series, however, it became clear that the difference between the two kinds of ulceration was real. As before, a simple way of looking at the overall findings up to the present time is to add all the figures for gastric ulcer and compare the percentage frequencies with control frequencies obtained by weighting the controls according to the number of patients with gastric ulcer at each centre (Table V).

TABLE V

GASTRIC ULCER

Brief Summary of Results from Nine Areas shown separately in Tables VI and VII

| Blood Group | Gastric Ulcer | | Control* Percentages | Corresponding Duodenal Ulcer* Percentages | Per cent. Increase or Decrease | |
|---|---|---|---|---|---|---|
| | Numbers | Percentages | | | Of Gastric Ulcer on Controls | Of Gastric Ulcer on Duodenal Ulcer |
| O | 1,903 | 47·59 | 43·33 | 51·26 | + 9·8 | −7·2 |
| A | 1,597 | 39·93 | 42·25 | 36·54 | − 5·5 | +9·3 |
| B | 351 | 8·78 | 10·38 | 8·59 | −15·4 | +2·2 |
| AB | 148 | 3·70 | 4·04 | 3·61 | − 8·4 | +2·5 |
| Total .. .. | 3,999 | | | | | |

* Weighted according to number of patients with gastric ulcer at each centre.

The nine centres shown in Table V are the same for both kinds of ulceration, so that corresponding weighted percentages, calculated in the same way, can be shown for duodenal ulcer.

The result is quite clear. With gastric ulcer the proportion of persons belonging to Group O is increased and all the other groups are diminished. The numbers are smaller, however, than for duodenal ulcer and in addition the differences are proportionately less. Hence the figures are rather more irregular than those for duodenal ulcer given in the preceding section. The comparison with duodenal ulcer shows a lower proportion of Group O and a higher proportion of all the other groups. In fact, the figures for gastric ulcer are about intermediate between duodenal ulcer and the controls.

The analysis for gastric ulcer and controls is shown in Table VI. The comparisons are O : A and O : (A + B + AB). Though the evidence for a greater incidence in Group O is not so overwhelming as in duodenal ulcer, it is overwhelming enough. The mean weighted relative incidence of gastric ulcer in persons of Group O, taken over all the centres, is 1·16 as against persons of Group A, and 1·19 as against persons of the other three groups added together. The areas are perfectly homogeneous.

An analysis of the difference between the two kinds of ulceration is shown in Table VII.

TABLE VI*

GASTRIC ULCER

Analysis of Incidence of Disease in Persons of Group O Relative to its Incidence in Persons of the Other Groups

| | Centre | No. in Disease Series | Relative Incidence O : A | $\chi^2$ | Relative Incidence O : (A+B+AB) | $\chi^2$ |
|---|---|---|---|---|---|---|
| 1 | London | 599 | 1·27 | 7·08 | 1·30 | 9·98 |
| 2 | Manchester | 232 | 1·13 | 0·77 | 1·18 | 1·61 |
| 3 | Newcastle | 184 | 1·40 | 4·23 | 1·31 | 3·36 |
| 4 | Liverpool | 438 | 0·96 | 0·16 | 1·01 | 0·00 |
| 5 | Glasgow | 300 | 1·16 | 1·24 | 1·18 | 1·96 |
| 6 | Copenhagen | 337 | 1·22 | 2·79 | 1·26 | 3·66 |
| 7 | Oslo | 412 | 1·25 | 4·45 | 1·26 | 5·27 |
| 8 | Vienna | 1,028 | 1·09 | 1·26 | 1·09 | 1·48 |
| 9 | Iowa | 469 | 1·23 | 4·19 | 1·33 | 8·73 |
| Total | | 3,999 | | | | |
| Mean Weighted Relative Incidence | | | 1·16 | | 1·19 | |
| $\chi^2$ | Total | | | 26·18 | | 36·05 |
| | Difference from Unity, D. of F. = 1 | | | 18·54 | | 27·65 |
| | Heterogeneity, D. of F. = 8 | | | 7·64 | | 8·40 |
| *P* | Heterogeneity | | | 0·5 | | 0·4 |

TABLE VII*

COMPARISON OF GASTRIC AND DUODENAL ULCER

Relative Incidence of Duodenal Ulcer in Patients of Group O as against the Incidences shown for Gastric Ulcer

| | Centre | No. of Patients with Duodenal Ulcer | No. of Patients with Gastric Ulcer | Relative Incidence O : (A+B+AB) | $\chi^2$ |
|---|---|---|---|---|---|
| 1 | London | 946 | 599 | 1·18 | 2·53 |
| 2 | Manchester | 423 | 232 | 1·02 | 0·02 |
| 3 | Newcastle | 482 | 184 | 1·19 | 1·02 |
| 4 | Liverpool | 1,059 | 438 | 1·53 | 13·82 |
| 5 | Glasgow | 1,642 | 300 | 0·99 | 0·01 |
| 6 | Copenhagen | 680 | 337 | 1·17 | 1·44 |
| 7 | Oslo | 579 | 412 | 1·24 | 2·67 |
| 8 | Vienna | 1,160 | 1,028 | 1·12 | 1·79 |
| 9 | Iowa | 1,301 | 469 | 1·03 | 0·08 |
| Total | | 8,272 | 3,999 | | |
| Mean Weighted Relative Incidence | | | | 1·17 | |
| $\chi^2$ | Total | | | | 21·60 |
| | Difference from Unity, D. of F. = 1 | | | | 12·09 |
| | Heterogeneity, D. of F. = 8 | | | | 9·51 |
| *P* | Heterogeneity | | | | 0·3 |

* Sources of material as in Table III.

The comparison is in terms of O : (A+B+AB), and what is shown this time is the relative incidence of duodenal ulcer in patients of Group O, not as against the controls, but as against patients at the same centres with gastric ulcer. There is strong evidence that the difference between the two types of ulceration is real, and, once again, on these numbers, the nine centres give no indication at all of significant heterogeneity.

The results of this section are instructive in the clear indications they give for the need for large numbers. Some of the writers have been concerned by the apparent variation shown by the different series. Thus, with 438 patients at Liverpool, the figures for gastric ulcer are almost identical with those for the controls. At Manchester, Glasgow, and Iowa, the excess of Group O is fully as great as in duodenal ulcer. Nevertheless, when all the series are combined, there is no indication of any significant heterogeneity. This kind of variation is only to be expected with series of these orders of magnitude. It is fortunate that ABO blood-grouping is now so uniformly reliable, and that the requirements for obtaining suitable controls are so well understood, that series from different centres, collected by different workers, can be safely compared and combined. It is the larger figures for duodenal ulcer that are significantly heterogeneous, though, because the excess of Group O appears in some degree at all centres, this is not immediately obvious and has invited little or no discussion. It may well be that, when much larger numbers are available for gastric ulcer, significant heterogeneity will duly appear, but that time is not yet.

It is far from easy to classify ulcers situated near the pylorus and it might be suggested that the apparent excess of Group O in gastric ulcer is due to some degree of misclassification of ulcers which should have been called duodenal, or omitted altogether for safety. It would seem, however, that the excess of Group O in gastric ulcer is altogether too large for this; a 50 per cent. misclassification would be needed to account for the findings.

As with duodenal ulcer, no subdivision of the material has as yet revealed differences in blood group proportions, apart from the quite remarkable findings of Billington (1956b). In a series of 237 patients at Sydney, he had these results:

| Type of Ulcer | Group | | | |
|---|---|---|---|---|
| | O | A | B | AB |
| Prepyloric .. .. .. | 22 | 52 | 7 | 2 |
| Non-prepyloric .. .. | 94 | 47 | 11 | 2 |
| Total Gastric Ulcers .. | 116 | 99 | 18 | 4 |

Turning these figures into percentages and comparing with the control series, the figures are:

| Type of Ulcer | Group Percentages | | | |
|---|---|---|---|---|
| | O | A | B | AB |
| Prepyloric .. .. .. | 26·5 | 62·7 | 8·4 | 2·4 |
| Non-prepyloric .. .. | 61·1 | 30·5 | 7·1 | 1·3 |
| Total Gastric Ulcers .. | 48·9 | 41·8 | 7·6 | 1·7 |
| Controls .. .. .. | 48·9 | 38·4 | 9·7 | 3·0 |

The total frequencies are close to those of the controls, but the enormous excess of Group A in prepyloric ulcers and of Group O in the remainder are both very highly significant. It is greatly to be hoped that further studies will soon be forthcoming, but in the meantime it is desirable to suspend judgment, as indeed Billington himself rather suggests. He was faced with the difficulties of classifying the ulcers retrospectively from hospital notes and many doubtful cases had to be omitted. It should also be said that the cases of Clarke and others (1955) which were classified as juxtapyloric, though not very numerous, are fully as high in Group O as their cases of duodenal ulcer, and that a small series of ulcers classified as prepyloric in the material of Aird and others (1954) gave nineteen Os, eleven As, and two Bs. Both these findings are entirely at variance with Billington's extraordinary excess of Group A, both differences being highly significant.

### (5) Cancer of the Stomach

A summary of results is given in Table VIII (opposite). Amongst patients the proportion of Group A is increased, the proportions of Groups O and B both being decreased. On these numbers nothing definite can be said about Group AB.

The analysis is shown in Table IX (opposite). The results are unequivocal; the relative incidence of the disease is greater, with very high significance, in

TABLE VIII

CANCER OF THE STOMACH

Brief Summary of Results from Thirteen Centres shown separately in Table IX

| Blood Group | Cancer of Stomach | | Control* Percentages | Per cent. Increase or Decrease on Controls |
|---|---|---|---|---|
| | Numbers | Percentages | | |
| O | 2,795 | 41·13 | 44·43 | − 7·4 |
| A | 3,127 | 46·02 | 41·86 | +10·0 |
| B | 606 | 8·92 | 9·88 | − 9·7 |
| AB | 267 | 3·93 | 3·83 | + 2·6 |
| Total | 6,795 | | | |

Approximate Relative Incidences:

A : O, 1·19; A : B, 1·22; O : B, 1·03;

* Weighted according to number of patients with cancer of the stomach at each centre.

persons of Group A as against persons both of Group O and Group B. The centres are not significantly heterogeneous. Once again we can conclude that there is no evidence to suggest that the thirteen centres are not uniform for the increase in Group A.

A point of interpretation arises here. Speiser (1956) concludes that his large series from Vienna does not confirm the findings at other centres. This is entirely correct; Vienna would certainly differ with fairly high significance from all the other areas taken together. But if there is no reason for choosing one particular result out of the thirteen, it is equally legitimate to say that a series, even of this size, may differ from the rest by chance, when the comparison is one arbitrarily selected from many that could be made. A mere inspection of the relative incidences reveals a very reasonable uniformity, and out of thirteen results there is not one that, for the more reliable A : O comparision, shows a higher proportion of O than of A in the disease series as against the controls. It would be interesting to know whether the incidence of the disease is raised in persons of Group AB, but much larger numbers will be required before this point can be decided.

With one exception, no evidence has yet appeared that subdivision of the material yields significant differences. The exception is once again the site of the lesion. Jennings, Balme, and Richardson (1956) analysed results for 254 patients treated by partial or total gastrectomy, and found a large excess of Group A in those in whom the tumour was situated at the pylorus, a moderate excess of Group A when the tumour was at the cardia, and equality of Groups O and A when the site was the body of the stomach. Billington (1956c) also found an excess of Group A in prepyloric and cardiac cancers and a very large

TABLE IX

CANCER OF STOMACH

Analysis of Incidence of Disease in Persons of Group A Relative to the Incidence in Persons of Group O and Group B

| | Centre | No. in Disease Series | Relative Incidence A : O | $\chi^2$ | Relative Incidence A : B | $\chi^2$ |
|---|---|---|---|---|---|---|
| 1 | London | 1,340 | 1·16 | 5·67 | 1·23 | 3·39 |
| 2 | London | 97 | 1·80 | 6·70 | * | * |
| 3 | Manchester | 770 | 1·22 | 6·39 | 1·49 | 6·34 |
| 4 | Newcastle | 101 | 1·25 | 1·12 | * | * |
| 5 | Liverpool | 217 | 1·31 | 2·75 | 0·87 | 0·34 |
| 6 | Birmingham | 100 | 1·60 | 4·46 | * | * |
| 7 | Leeds | 217 | 1·31 | 3·52 | 1·22 | 0·50 |
| 8 | Glasgow | 299 | 1·09 | 0·45 | 1·16 | 0·48 |
| 9 | Basel | 704 | 1·36 | 12·16 | 1·41 | 4·90 |
| 10 | Copenhagen | 413 | 1·39 | 8·75 | 1·19 | 1·08 |
| 11 | Vienna | 1,146 | 1·00 | 0·00 | 1·07 | 0·49 |
| 12 | Iowa | 908 | 1·20 | 5·61 | 1·08 | 0·32 |
| 13 | Sydney | 483 | 1·06 | 0·41 | 1·39 | 3·24 |
| Total | | 6,795 | | | | |
| Mean Weighted Relative Incidence | | | 1·19 | | 1·19 | |
| $\chi^2$ | Total | | | 57·99 | | 21·09 |
| | Difference from Unity, D. of F. =1 | | | 39·64 | | 13·66 |
| | Heterogeneity, D. of F. =12 | | | 18·36 | | |
| | Heterogeneity, D. of F. =9 | | | | | 7·43 |
| *P* | Heterogeneity | | | 0·1 | | 0·6 |

* Numbers too small.

*Note:* Control figures for Glasgow are from a new and improved series subsequently published by Brown, Melrose and Wallace (1956).

(1, 3–7) Aird, Bentall, and Roberts (1953); (10) Køster, Sindrup, and Seele (1955);
(2) Walther, Raeburn, and Case (1956); (11) Speiser (1956);
(8) Wallace (1954); (12) Buckwalter, Wohlwend, Colter, Tidrick, and Knowler (1956a);
(9) Dr. L. P. Holländer of Basel, *cited by* Aird and others (1953); (13) Billington (1956c)

excess of Group O in cancers of the body of the stomach. The results for O and A in the two investigations are as follows:

| Site of Cancer | Authors and Date | | | |
|---|---|---|---|---|
| | Jennings and others (1956) | | Billington (1956c) | |
| | O | A | O | A |
| Pylorus and Antrum .. | 33 | 64 | 53 | 96 |
| Body of the Stomach .. | 41 | 42 | 154 | 47 |
| Cardia .. .. .. | 15 | 22 | 24 | 50 |

With differences of this magnitude, moderate differences in control frequencies are of little moment. The percentages of Groups O and A may be taken as 46 and 42 for London, and 49 and 38 for Sydney. The two series are in close agreement for prepyloric cancers and not significantly different for cancers of the cardia. The figures for cancer of the body of the stomach are, however, utterly discrepant. The total result is that in Billington's series there is little difference from the controls, whereas in that of Jennings and others there is a large excess of Group A. Incidentally, the figures of Jennings and others cannot be included in Tables VII and IX, as some of the cases have already been included in the figures for London published by Aird and others (1953). In this instance, too, it would be unsafe to come to any conclusion, and it is greatly to be hoped that further data bearing on the point will be forthcoming. The partial agreement of these two independent studies lends considerable weight to the findings, but the failure of the series of Jennings and others to confirm the extraordinary excess of Group O in cancer of the body of the stomach in the Sydney series makes caution desirable.

### (6) Pernicious Anaemia

With a relatively rare disease, and one for which routine blood-grouping may often not be carried out, it is difficult to secure the numbers required. Nevertheless, the evidence has now accumulated to the point at which it may be said with considerable confidence that patients suffering from this disease are unduly high in Group A. Table X gives, as before, a brief summary of results set out in more detail later.

Group A is increased, Groups O and B being correspondingly diminished, and to very much the same extent. The figures for Group AB are, of course, far too small to reveal anything.

Table XI gives the analysis for the comparision of Groups O and A. It will be noted that in London and Glasgow certain hospitals are left separate. This was because discrepant results seemed to be emerging and it seemed desirable not to risk masking a real heterogeneity that might be present. Actually, however, there is no significant heterogeneity. The $\chi^2$ for the difference from unity of 16·54 for one degree of freedom leaves little doubt about the reality of the association. The comparison of Groups A and B has not been made; with these very small series special methods would have to be used. But the close similarity of the relative incidences

Table X

Pernicious Anaemia

Brief Summary of Results shown separately in Table XI

| Blood Group | Pernicious Anaemia | | Control* Percentages | Per cent. Increase or Decrease on Controls |
|---|---|---|---|---|
| | Numbers | Percentages | | |
| O | 636 | 42·46 | 47·00 | − 9·7 |
| A | 685 | 45·73 | 40·30 | +13·5 |
| B | 126 | 8·41 | 9·36 | −10·1 |
| AB | 51 | 3·40 | 3·34 | + 1·8 |
| Total | 1,498 | | | |

Approximate Relative Incidences:

A : O, 1·26; A : B, 1·26; O : B, 1·01;

* Weighted according to number of patients at each centre.

Table XI

Pernicious Anaemia

Analysis of Incidence of Disease in Persons of Group A Relative to its Incidence in Persons of Group O

| | Centre* | No. in Disease Series | Relative Incidence A : O | $\chi^2$ |
|---|---|---|---|---|
| 1 | London (Hammersmith .. | 134 | 1·70 | 8·05 |
| 2 | London (Kingston .. .. | 68 | 1·98 | 6·90 |
| 3 | London (Others .. .. | 42 | 1·03 | 0·01 |
| 4 | Oxford .. .. .. | 258 | 1·09 | 0·41 |
| 5 | Cambridge .. .. .. | 110 | 1·01 | 0·00 |
| 6 | Sheffield .. .. .. | 123 | 1·36 | 2·35 |
| 7 | Newcastle .. .. .. | 109 | 1·03 | 0·02 |
| 8 | Glasgow (Southern General | 110 | 0·93 | 0·13 |
| 9 | Glasgow (Royal Infirmary .. | 160 | 1·41 | 3·83 |
| 10 | Copenhagen .. .. .. | 111 | 0·98 | 0·01 |
| 11 | Iowa .. .. .. .. | 158 | 1·42 | 3·97 |
| 12 | San Francisco .. .. .. | 115 | 1·70 | 6·96 |
| Total .. .. .. .. | | 1,498 | | |
| Mean Weighted Relative Incidence .. | | | 1·26 | |
| $\chi^2$ | Total .. .. .. .. .. | | | 32·64 |
| | Difference from Unity, D. of F. = 1 | | | 16·54 |
| | Heterogeneity, D. of F. = 11 .. .. | | | 16·10 |
| *P* | Heterogeneity .. .. .. | | | 0·14 |

*(1–9) *British Medical Journal* (1956);
(10) Køster, Sindrup, and Seele (1955);
(11) Buckwalter, Wohlwend, Colter, Tidrick, and Knowler (1956 a);
(12) Creger and Sortor (1956).

makes it fairly certain that Groups O and B go together. A comparison of Group A against Groups O and B combined raises the $\chi^2$ for the difference from unity to 18·5 and still leaves the areas homogeneous. The figures of Buchanan and Higley (1921) as shown in Table I, cannot be included, as there are no controls, but they undoubtedly support the conclusion.

The difficulties and dangers of small numbers are even more clearly shown than by the larger series of the preceding sections. With numbers of this order there is nothing unexpected in getting individual incidences ranging from practically two to one down to an actual excess of Group O. Thus Creger and Sortor (1956) are concerned about the difference between their findings and those of Buchanan and Higley. Actually, the results agree as well as could reasonably be expected. Only when series are added together can clear conclusions be expected, and at the moment there is nothing to contradict at the conventional 5 per cent. level the hypothesis that all centres agree. But of course real discrepancies may emerge later; it will be time enough then to attempt to account for them.

### (7) Diabetes Mellitus

We now come to conditions for which the evidence is less strong, justifying no more than a provisional conclusion which may serve as a pointer to profitable work in the future. With diabetes mellitus, however, the evidence is fairly strong. The usual summary is given in Table XII.

TABLE XII

DIABETES MELLITUS

Brief Summary of Results from Centres shown separately in Table XIII

| Blood Group | Diabetes Mellitus | | Control* Percentages | Per cent. Increase or Decrease on Controls |
|---|---|---|---|---|
| | Numbers | Percentages | | |
| O | 990 | 46·05 | 49·12 | − 6·3 |
| A | 892 | 41·49 | 38·31 | + 8·3 |
| B | 183 | 8·51 | 9·58 | −11·2 |
| AB | 85 | 3·95 | 2·99 | +32·1 |
| Total | 2,150 | | | |

Approximate Relative Incidences:
A : O, 1·16; A : B, 1·22; O : B, 1·06

* Weighted according to number of patients at each centre.

Once again Group A is increased and Groups O and B both diminished and in very nearly the same proportion. On such numbers nothing can be said about the apparently high figure for AB in the disease series.

The detailed analysis is shown in Table XIII for Groups A and O. It will be seen that the $\chi^2$ for the difference from unity is 9·2 and the four areas are perfectly homogeneous. The addition of Group B to Group O would increase the figure appreciably, so it may be concluded that there is strong, though by no means overwhelming, evidence, that diabetes mellitus is indeed commoner in those belonging to Group A. The evidence is less strong than for pernicious anaemia, although the numbers are considerably larger. This is because the excess in Group A is a good deal less.

TABLE XIII

DIABETES MELLITUS

Analysis of Incidence of Disease in Persons of Group A Relative to its Incidence in Persons of Group O

| | Centre* | No. in Disease Series | Relative Incidence A : O | $\chi^2$ |
|---|---|---|---|---|
| 1 | S.W. Lancashire .. | 634 | 1·12 | 1·71 |
| 2 | W. Cheshire .. .. | 199 | 1·19 | 1·39 |
| 3 | Oxford .. .. | 500 | 1·11 | 1·49 |
| 4 | Glasgow .. .. | 817 | 1·20 | 5·02 |
| Total .. .. .. | | 2,150 | | |
| Mean Weighted Relative Incidence .. | | | 1·16 | |
| $\chi^2$ | Total .. .. .. .. | | | 9·61 |
| | Difference from Unity, D. of F. = 1 | | | 9·20 |
| | Heterogeneity, D. of F. = 3 .. | | | 0·41 |
| *P* | Heterogeneity .. .. .. | | | 0·9 |

**Note:* Control figures for Glasgow are from a new and improved series published by Brown, Melrose, and Wallace (1956).

(1–3) McConnell, Pyke, and Roberts (1956).
(4) Craig ahd Wang (1955).

McConnell, Pyke, and Roberts (1956) provide a useful warning of the dangers inherent in this type of work at the stage when differences are only moderately significant. They found in the first three areas of Table XIII that the excess of Group A was entirely confined to men. A direct comparison of the sexes was moderately significant and these matters were discussed at length. The results of Craig and Wang (1955) for Glasgow showed the same excess of Group A, but in that instance it occurred in women only. Combining the figures from the four centres, the sex difference became non-significant. In these 2,000 observations there is nothing appreciable to contradict the hypothesis that the excess occurs in both men and women, and also that it is present, and to an equal degree, over all ages at onset of the disease.

### (8) Bronchopneumonia in Infants

Struthers (1951) determined the ABO blood group frequencies in 400 consecutive cases coming to *post-mortem* examination at the Royal Hospital for Sick Children, Glasgow. 320 were under the age of 2 years. In 148 the diagnosis of bronchopneumonia was confirmed histologically, 55 having no other apparent abnormality. These children showed a very low frequency of Group O and a high frequency of the other groups. The remaining 252 gave frequencies very similar to a control series of blood donors. The results are summarized in Table XIV.

Table XIV

BRONCHOPNEUMONIA IN INFANTS

Data on 400 Consecutive *post-mortem* Examinations (Struthers, 1951)

| Blood Group | Controls | | Bronchopneumonia | | | |
|---|---|---|---|---|---|---|
| | | | Present | | Not Present | |
| | Numbers | Percentages | Numbers | Percentages | Numbers | Percentages |
| O | 3,063 | 50·9 | 47 | 31·8 | 126 | 50·0 |
| A | 2,115 | 35·2 | 68 | 45·9 | 90 | 35·7 |
| B | 654 | 10·9 | 21 | 14·2 | 29 | 11·5 |
| AB | 179 | 3·0 | 12 | 8·1 | 7 | 2·8 |
| Total | 6,011 | | 148 | | 252 | |

The difference between the controls and the bronchopneumonia series is highly significant. Comparing Os and non-Os in a four-fold table, $\chi^2$ is 20·54 for one degree of freedom. It will be noted that, small though the numbers are, there is an indication that, in addition to Group A, Groups B and AB are also increased.

This work has been repeated by Carter and Heslop (1957) on a somewhat larger series from London. Owing to the great reduction in deaths of infants from bronchopneumonia, however, the new sample corresponds only to that part of Struthers' material in which bronchopneumonia was an associated finding. The London series shows no significant difference from the controls. Using all Struthers' 148 cases, the difference between the two series is significant, but this is not so if the 55 dying of bronchopneumonia are omitted. While it seems likely that the London and Glasgow series are in definite disagreement, it would be premature to conclude that there is not a real phenomenon to be investigated and it is to be hoped that further studies will be carried out.

### (9) Pituitary Adenoma

Mayr, Diamond, Levine, and Mayr (1956) have studied the blood-group frequencies in patients suffering from brain tumours and pituitary adenomata. With 637 brain tumours of various kinds the frequencies were closely similar to those of a large control series for Boston. 123 pituitary adenomata, however, gave a very different result, the frequencies being: O, 74; A, 24; B, 19; AB, 6. The excess of Group O and deficiency of Group A are very highly significant. As some patients came from places remote from Boston, and two New York Hospitals were also added, the authors have preferred to compare the pituitary adenomata with the other patients with brain tumours, who were selected in the same way. Even these limited figures yield a $\chi^2$ of 9·97 when Group O is compared with the sum of the other groups, and 18·45 when Group A is similarly compared with the sum of the other groups (both for one degree of freedom).

Much weight is added to the result by the correspondence between the figures from the six different hospitals, four at Boston and two at New York. Apart from one hospital which contributed only four cases, the other five were in complete agreement in showing very high numbers of Group O and very low numbers of Group A. The authors are cautious and say that it is advisable to consider the findings as tentative, but they have certainly put forward a strong case, and it is greatly to be hoped that confirmation will be sought at other centres.

### (10) Portal Cirrhosis

Billington (1956a) examined the records of 111 cases, mostly blood-grouped because they had bleeding oesophageal varices. There was a marked excess of Group A, the figures being: O, 37; A, 65; B, 7; AB, 2. Control frequencies were: O, 14,672; A, 11,514; B, 2,912; AB, 902. $\chi^2$ for the comparison of Groups O and A, with one degree of freedom, was 17·12. A series of 149 patients with bronchiectasis gave entirely normal frequencies. There might possibly be some connexion here with Buchanan and Higley's figures for "Jaundice, All Causes" as shown in Table I; these indicate a large number of Group A. Nevertheless, as Mayr and others (1956) remarked about their findings with pituitary adenoma, it is well to regard such results, whatever their apparent significance, as tentative until they are confirmed at other centres and on larger numbers.

### (11) Rheumatic Fever

Glynn, Glynn, and Holborow (1956) found 124 non-secretors amongst 450 children with rheumatic fever (27·6 per cent.). In 460 healthy schoolchildren 100 (21·7 per cent.) were non-secretors. The difference just attains the 5 per cent. level of significance.

### (12) Three Negative Results

*Cancer of the Colon and Rectum, Lung, and Breast*

It would be disturbing and suspicious if almost all diseases were to show blood-group associations. When positive findings appear it is reassuring to get completely negative results for other diseases. This is especially true when positive and negative results are found by the same workers at the same hospitals. The negative series of patients from the same hospitals also serve as second-line controls, confirming the results obtained by using control series of blood donors. The three conditions described in this section have all been studied at several centres and on fairly large numbers of patients. The results are shown in Table XV, which gives incidences in persons of Group A relative to that in persons of Group O.

The $\chi^2$'s for the difference from unity are all non-significant and the centres are perfectly homogeneous in all three instances. It will be noted, however, that there is one result individually significant at the 5 per cent. level. This is an excess of O in cancer of the breast at Iowa. But, of course, one such result out of eighteen is close to expectation at this level of significance.

It will be further noted that even with numbers ranging from 2,000 to 3,000 the approximate 95 per cent. fiducial limits are still fairly wide. The three results are certainly negative on these numbers, but a rather small association is not excluded. Negative results, too, need large numbers if they are to be established with confidence. It is permissible, perhaps, as an illustration, to combine all three diseases. If this is done, $\chi^2$ for the difference from unity is 1·24 for one degree of freedom and $\chi^2$ for heterogeneity is 3·91 for five degrees of freedom. The mean weighted relative incidence is 1·03, and with 7,600 in the disease series the 95 per cent. fiducial limits are down to the fairly close bracket 0·98–1·09.

### (13) Further Negative Results

Pike and Dickins (1954) studied a series of women suffering from toxaemia of pregnancy and found a significant excess of Group O. Further work at the same hospital, however (Dickins, Richardson, Pike, and Roberts, 1956) did not confirm the previous findings, the combined data now yielding a negative result. Pearson and Pinker (1956) also obtained a negative result. The combined series comprised 1,385 patients and following the methods of this paper $\chi^2$ for the difference from unity is 0·07. The two series, however, are just significantly heterogeneous, $\chi^2$ being 5·36 for one degree of freedom. Actually, one series gives an excess of O, the other of A, but these cancel out when the figures

TABLE XV

CANCER OF COLON AND RECTUM, OF LUNG, AND OF BREAST

Analysis of Incidence of Disease in Persons of Group A Relative to the Incidence in Persons of Group O

| | Centre* | Cancer of Colon and Rectum | | | Cancer of Lung | | | Cancer of Breast | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. in Disease Series | Relative Incidence A : O | $\chi^2$ | No. in Disease Series | Relative Incidence A : O | $\chi^2$ | No. in Disease Series | Relative Incidence A : O | $\chi^2$ |
| 1 | London | 1,514 | 1·10 | 2·80 | 384 | 1·06 | 0·26 | 85 | 1·12 | 0·21 |
| 2 | Manchester | 359 | 1·12 | 0·97 | 340 | 1·05 | 0·17 | 325 | 0·96 | 0·11 |
| 3 | Birmingham | 520 | 0·99 | 0·00 | 274 | 0·89 | 0·63 | 502 | 0·98 | 0·04 |
| 4 | Newcastle | 206 | 1·00 | 0·00 | — | — | — | 105 | 1·02 | 0·01 |
| 5 | Liverpool | — | — | — | 939 | 0·95 | 0·44 | — | — | — |
| 6 | Iowa | 256 | 0·95 | 0·12 | 395 | 0·79 | 4·62 | 866 | 1·14 | 2·86 |
| 7 | London (2) | 185 | 1·03 | 0·04 | 184 | 1·15 | 0·77 | 137 | 1·24 | 1·28 |
| Total | | 3,040 | | | 2,516 | | | 2,020 | | |
| Mean Weighted Relative Incidence | | | 1·06 | | | 0·96 | | | 1·07 | |
| 95 per cent. Fiducial Limits | | | 0·98–1·15 | | | 0·88–1·05 | | | 0·97–1·18 | |
| $\chi^2$ | Total | | | 3·93 | | | 6·89 | | | 4·50 |
| | Difference from Unity, D. of F. = 1 | | | 2·15 | | | 0·80 | | | 1·65 |
| | Heterogeneity, D. of F. = 5 | | | 1·78 | | | 6·09 | | | 2·85 |
| *P* | Heterogeneity | | | 0·9 | | | 0·3 | | | 0·7 |

*(1–4) Aird, Bentall, Mehigan, and Roberts (1954)
(5) McConnell, Clarke, and Downton (1954)
(6) Buckwalter, Wohlwend, Colter, Tidrick, and Knowler (1956 a);
(7) Walther, Raeburn, and Case (1956).

are combined. The individual $\chi^2$'s for the two series do not attain significance.

Maxwell and Maxwell (1955) published results for 2,147 patients with hypertension. The O : A ratio was almost identical in patients and controls. It was pointed out, however, by Aird, Bentall, and Roberts (1955) that there is a curious and indeed significant deficiency of AB's amongst the men, which might just possibly be meaningful. Trobridge (1956) obtained a negative result in 1,400 patients with tuberculosis. His findings for Rhesus are mentioned later.

Smaller series have appeared for a number of other diseases, showing no significant differences from controls. They will be very useful when further results appear and can be added, for though the findings are negative at present, quite sizeable associations cannot be ruled out when numbers are small.

### (14) The Rhesus System

The only results available up to the present refer to the simple division into Rh positive and Rh negative. Results for relatively large series of patients with gastro-duodenal ulcer, cancer of the stomach, cancer of the colon and rectum, cancer of the lung, and cancer of the breast, have been published by Aird and others (1954), Clarke and others (1955), Buckwalter and others (1956a, b), Speiser (1956), and others. These results are all negative. The frequencies observed either agree with those in control series or are in reasonable agreement with the frequencies to be expected in the population concerned. With Rhesus, unlike ABO, there are difficulties about contrasting the results of workers at different laboratories, and suitable controls are not so easily obtained.

Apart from the negative results for relatively large numbers there are one or two papers in which claims for association are made. In view, however, of some uncertainties as to how the data were collected, and of the fact that there are discrepancies in population results from different centres, with the doubt this raises about possible small differences in technique, it seems better to suspend judgment for the present. These findings are not dealt with, as it would require much space to elaborate objections, and it would be ungracious to criticize work without setting out objections in detail.

One finding, however, requires special mention. Trobridge (1956) examined ABO and Rhesus frequencies (positive and negative) in patients suffering from tuberculosis. As already mentioned, the results for ABO were negative, but the Rhesus findings are suggestive. The patients were drawn from the five south-western counties of England, and Trobridge used as controls blood donors grouped by the National Blood Transfusion Service. He was careful to check his technique against theirs and a sample of patients was grouped by both, without any discrepancy appearing. In 1,362 patients the percentage who were Rh negative was 22·54 against 18·69 in 9,066 controls. The figures for the controls, however, show significant heterogeneity as between the five counties. So applying the method used throughout this paper and treating the counties separately, it is found that the mean weighted relative incidence of tuberculosis in persons who are Rh negative is 1·25. $\chi^2$ for the difference from unity is 9·84 for one degree of freedom; and for heterogeneity 3·80 for four degrees of freedom. So there is at least a strong suggestion that tuberculosis may be commoner in those who are Rhesus negative.

### (15) Subdivisions and the Other Blood-Group Systems

It would be very interesting to discover whether, for example, the excess of Group A in patients suffering from cancer of the stomach or pernicious anaemia applied both to $A_1$ and $A_2$. A search for disease associations with the subdivisions of Rhesus and also with all the other blood-group systems is of great potential interest. No result on adequate numbers are yet available, however. Nevertheless, a beginning has been made. Data are being recorded, and in due course we may look forward to a substantial extension of the subject. For example, Walther, Raeburn and Case (1956) have published results for 1,000 patients suffering from malignant disease of various kinds, showing groupings for ABO, including the subdivision of A into $A_1$ and $A_2$, Rh+ and Rh−, MN, and secretor status. In due course numbers will become adequate, and in view of past experience no one can foretell what discoveries may not be made.

### (16) Comment

Some associations between blood groups and disease are now known to exist, and others are probable. In considering what they imply there are, broadly, three possibilities. In the first place, the associations might in a sense not be real at all; they might be secondary to stratifications within the population. Secondly, the differing susceptibilities might be pleiotropic effects of the blood-group genes, that is, some other and different effect from that of their role in determining the presence of the antigens. Thirdly, the associations might depend upon the

physical presence of the blood-group substances, though this action need not necessarily be antigenic.

To take the first possibility, suppose we had a mixed population of Eastern Europeans with dark hair and of largely fair-haired Northern Europeans, then if blood-grouping were carried out it would be found that dark hair was associated with Group B. But, of course, this would merely be secondary to the racial difference. The associations with disease cannot be explained on a racial basis, but, it could be asked, might there not be within populations strains who were at the same time high in Group O and unduly susceptible to duodenal ulceration, and other strains relatively high in A and especially resistant to that disease? There are a number of considerations which seem to make this stratification hypothesis unlikely. First of all, it would be very curious if the same kind of stratifications existed in the very different populations of the various countries in which the associations have been found. In the second place, there is no evidence that stratifications for blood-group frequencies do in fact exist. On the contrary, such evidence as there is points to homogeneity of populations. Moreover, the differences in blood-group frequencies between the hypothetical strata would have to be relatively enormous to account for associations of the magnitude of that found, for example, with duodenal ulcer. Nevertheless, a more direct test of the stratification hypothesis is very desirable, and this is what Clarke and others (1956) have carried out by comparing duodenal ulcer patients with their own brothers and sisters.

Clarke and others (1956) grouped 293 sibships of brothers and sisters, each starting with a patient, a propositus, with duodenal ulcer. Unfortunately, the many sibships in which all the members belong to the same blood group cannot give any information. But those which contain both Os and non-Os can be analysed. The method used is due to C. A. B. Smith. It is simple and efficient; for full details the paper of Clarke and his co-workers may be consulted. Briefly, if we think of a sibship of two, one O, one non-O, then on the null hypothesis that there is no association within sibships between blood group and ulcer, the propositus with the ulcer who brings this segregating sibship into the record has an equal chance of being O or non-O. Probabilities are computed in the same way for different sizes and compositions of sibships. There were 112 segregating sibships and the propositus was of Group O in 59 instances. The expected number, on the null hypothesis of no association, was 54·9095, the difference being only 0·804 times its standard error. It was therefore concluded that there was no evidence that persons of Group O are any more likely to develop ulcer than their own non-O sibs. Actually, however, while this is true, the numbers are insufficient for any conclusion either way. As pointed out by Roberts (1957), the calculation may be repeated using probabilities calculated on the basis of a relative incidence of ulcer in Os of 1·54, which is the figure indicated for Liverpool by the previous survey of Clarke and others (1955). The expected number is now 65·989; the difference from the observed 59 is 1·39 times its standard error and so non-significant at the 5 per cent. level. In fact, the data do not contradict at this level of significance any figure for relative incidence in Os which does not exceed 1·71, which is far higher than the mean figure of 1·38 shown in Table III, and considerably higher than the figure at any single centre.

Hence in regard to ABO blood groups the data of Clarke and others (1956), though an admirable beginning, will have to be supplemented by further observations before it can be decided whether the association observed in the general population also holds or does not hold within sibships of brothers and sisters.

With secretion, however, the result is conclusive. In 89 sibships segregating for secretion, the propositus was a non-secretor in 52 instances against an expectation of 42·464 on the null hypothesis of no association within sibships. The difference is 2·13 times its standard error. Roberts (1957) has pointed out, however, that sex should not be ignored. In England duodenal ulceration is about six times commoner in men than women. Thus if we consider a mixed sibship of two, one secretor and one non-secretor, one with ulcer and one normal, the propositus with the ulcer will nearly always be the man, whatever his secretor status. The simple plan is to consider only sibs of the same sex as the propositus. When this is done with Clarke's data 53 segregating sibships are left. The propositus is a non-secretor in 38 instances against an expectation of 24·900, The difference is now 3·72 times its standard error, corresponding to a probability of 1 in 5,000. There is thus extremely strong evidence that the association between ulcer and non-secretion holds within sibships of brothers and sisters as well as in the general population, and the hypothesis of stratification can be ruled out.

Incidentally, using sibships of one sex only for the ABO comparison, the result is still in doubt; the observed figure lies between that expected on the null hypothesis and that on the hypothesis of a relative incidence of 1·54 in persons of Group O, and does not differ significantly from either.

To call the effect pleiotropic means no more than that the blood-group genes may have other functions, unsuspected hitherto. It seems quite possible, however, that the presence of the blood-group substances may be involved in some way. It is certainly true that nearly all the diseases with which associations have been found are diseases of, or closely associated with, the upper part of the gastro-intestinal tract, a region in which, in secretors, group specific substances are present in large amounts. There has been a considerable amount of speculation, which should serve to stimulate work in the future, but for the moment there is little more to say.

This paper has concentrated on the biometrical aspects of the problem. Here we see biometry performing its classical function of uncovering problems for study, and sometimes furnishing pointers to lines of investigation which may prove profitable. Clearly there is still much to be done on these lines. It would be very useful to have many more bodies of data from many more centres, both for diseases already investigated and for others. When sub divisions are thought of the numbers can hardly be too large; it will be difficult indeed to secure enough. Standard subdivisions by sex, age, and many other factors should always be made. Above all, there is subdivision by type of disease, by its severity, and by its site. Anything that shows a difference may be a pointer to researches which may elucidate the associations and may be useful in the study of disease.

Finally, the biological implications are considerable. Following Fisher (1930), a neutral gene is almost unthinkable. Most of the blood-group genes have seemed to some almost devoid of selective value. Yet they show a polymorphism which must be as old as the species. For the ABO groups are found in the anthropoid apes. A long continued polymorphism must be dynamic, not static. It must depend on an interplay of selective advantages and disadvantages. Here, for the ABO system is a possible mechanism, for if the associations are truly causal, they are very large associations indeed. They fit in with the ideas of Mourant (1954), who has noted that while most of the blood group systems show variations in frequency which are continental, or sub-continental, the ABO system shows variation over much smaller areas. This suggests the operation of powerful selective factors. The balance is likely to be a nice one, however. All the evidence points to relative stability of frequencies over relatively short periods, and there seems to be every likelihood that the ABO system, to say nothing of the others, will maintain its usefulness in throwing light on the movements and inter-relationships of populations. But how far back it will be safe to go seems rather more uncertain than it did. It may be necessary to think in hundreds rather than in thousands of years.

## (17) Summary

There is overwhelming evidence that duodenal ulceration is about 40 per cent. commoner in persons of Group O than in persons of the other groups. This is the average figure for a number of centres in several different countries. Duodenal ulcer is also commoner in non-secretors of the ABO substances than in secretors. Gastric ulceration shows a higher relative incidence in persons of Group O, though it is not as high as with duodenal ulcer.

Cancer of the stomach and pernicious anaemia have a higher relative incidence in persons of Group A. Again, the evidence is exceedingly strong. There is fairly strong evidence for an association between Group A and diabetes mellitus. There is some evidence for further associations, but more investigations are needed before they can safely be accepted.

Negative results have been obtained for a number of other diseases, and for Rhesus with some of those mentioned.

It seems unlikely that the associations are secondary to stratifications in the populations studied. With duodenal ulcer and non-secretion stratification has been disproved. It may be that differing susceptibility to certain diseases is a pleiotropic effect of the blood-group genes. It seems even more probable that some direct physiological effect of the blood-group substances may be involved.

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# NATURE OF THE DETERMINANTS OF RHESUS ISOIMMUNIZATION

BY

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The circumstance necessary for the development of haemolytic disease of the newborn, the marriage of an Rh(D)-positive man to an Rh(D)-negative woman, is found in about 14 per cent. of all marriages, but only a small proportion of these result in an affected infant. This is because only about one woman of every twenty at risk develops immunity to her Rh-positive infants, for once immunity has developed all subsequent Rh-positive babies will be affected. It is not known why one mother should develop antibodies when nineteen fail to do so. ABO incompatibility between baby and mother reduces the risk still further, but as two-thirds of foetuses are compatible, this provides only a part explanation and has little bearing upon the main issue.

A first approach to the problem may be made in the following terms. We may ask whether the determining factors are present when the marriage is contracted and are intrinsic to the combination; or whether they are related to individual pregnancies, independently of the specific constitution of the marriage. If the first be true, then a prediction of the likelihood of haemolytic disease may eventually prove possible at the time of the marriage, and in the meantime failure of immunization in early pregnancies may be taken as reassurance for later ones. If the second be true, then no such prediction is possible, nor can early failure of immunization be regarded as more than an initial escape. Possibly both factors operate.

Fortunately, a study of the frequency-distribution of cases of haemolytic disease and particularly of "first affected" infants according to birth order, offers an approach to this question.

If predetermined factors were operating, this distribution would show a relative crowding of "first affected" infants in early pregnancies. If entirely predetermined, all the "first affected" infants of homozygous fathers would be second babies. If no predetermined factors operated, we could expect a relatively greater dispersion among later pregnancies. Different distributions can thus be expected according to whether one hypothesis or another is set up. These distributions are calculable and may be compared with the observed distribution.

## MATERIAL

During the periods July, 1947, to June, 1951, and January, 1953, to December, 1956, we recognized 920 "first affected" infants in Northumberland and Durham. For the purposes of the present study we think it reasonable to exclude sixteen first babies, and the remaining 904 were distributed according to their birth order as shown in Table I. We have omitted the period July, 1952, to December, 1952, because our records in this period included only treated cases, and these may be selected by birth order. On the other hand, we believe that the 904 cases in Table I are unselected. They were detected almost entirely upon the basis of routine

TABLE I

BIRTH ORDER OF 904 "FIRST AFFECTED" BABIES

| Birth Order .. | 2 | 3 | 4 | 5 | 6+7 | 8 or Later | Total |
|---|---|---|---|---|---|---|---|
| No. of Children | 392 | 261 | 121 | 74 | 33 | 23 | 904 |
| Percentage of Total .. | 43·4 | 28·9 | 13·4 | 8·2 | 3·7 | 2·5 | 100·1 |

antenatal antibody tests in Rh-negative women, or because a positive Coombs' test was found on the cord blood collected routinely from the infants of all Rh-negative women. Only about 10 per cent. were first suspected upon clinical grounds. ABO haemolytic disease has been excluded and a positive Coombs' test has been taken as defining the limits of the disease. By considering only "first affected" babies, the effect of a diseased child on family size has been avoided.

The proportion of cases ascertained in Northumberland and Durham during the above periods increased in the early years, but for the past 5 years has remained constant at five to six affected infants per 1,000 births. We calculate that over the whole period we have recognized at least 90 per cent. of all cases.

We therefore regard Table I as reliable. The 904 cases include stillbirths (8 per cent.) and the birth orders are calculated upon the basis of all previous children, stillborn, dead, and surviving, but excluding abortions. As we consider only "first affected" babies, we may presume that the death rate and stillbirth rate among previous children is the same as in the total population.

### Comparison with the Hypothetical Distributions

For comparison we propose a model in which the risk of an Rh(D)-negative women developing immunity is resolved into two parts: first, her initial susceptibility; second, her probability ($p$) of becoming sensitized to Rh-antigen at any given pregnancy. Of the two components, only $p$ is relevant to the determination of the birth order distribution. We suppose, for the time being, that initial susceptibility is an all-or-none phenomenon and divides the population into two distinct parts, that the value of $p$ is constant in the susceptible population and in successive pregnancies, and that sensitization is followed automatically by immunity to the next Rh(D)-positive foetus.

With a homozygous husband, there is a probability ($p$) that the first pregnancy will sensitize the wife, and a probability $(1 - p)$ of its not doing so. At the second pregnancy, there is a probability $p$ of an affected baby, a probability $p(1 - p)$ of sensitization, and a probability $(1 - p)^2$ of remaining unsensitized. Proceeding further, it can be shown that the probability that a baby of birth order "$n$" will be "first affected" is $p(1 - p)^{n-2}$. When $p$ equals 1, the series is 0, 1, 0, 0, 0 . . . . etc. When $p$ approaches zero, the series is $p$(0, 1, 1, 1, 1 . . . . etc.).

With a heterozygous husband, there is a probability $p/2$ of sensitization at the first pregnancy, and a probability $p/4$ that the second child will be affected. Also at the second pregnancy, there is a probability $\frac{p}{2}\left(1 - \frac{p}{2}\right)$ of sensitization, and a probability $\left(1 - \frac{p}{2}\right)^2$ of remaining unsensitized. Proceeding as in the last case, it can be shown that the probability of an affected baby is zero at the first pregnancy, and $\frac{x}{2} + \frac{p}{4}\left(1 - \frac{p}{2}\right)^{n-2}$ at subsequent pregnancies, where $x$ is the value calculated for the immediately preceding pregnancy. When $p$ equals 1, the series is $0, \frac{1}{4}, \frac{2}{8}, \frac{3}{16}, \frac{4}{32}$ . . . . etc., tending towards zero. When $p$ approaches zero, the series is $p\left(0, \frac{1}{4}, \frac{3}{8}, \frac{7}{16}, \frac{15}{32} \text{ . . . . etc.}\right)$ tending towards $\frac{p}{2}$.

We have computed the probabilities that children of different birth orders will be the "first affected" in a sibship at different levels of $p$, and have combined the values for D-homozygous and D-heterozygous husbands in the proportions of their occurrence in the general population, that is, 418 homozygous to 582 heterozygous (Mollison, Mourant, and Race, 1952). We have applied the results to the birth order distribution for the Northern Region of England in 1951, as shown in Table II, and have reduced the results to the percentage distributions which are given in Table III (Registrar-General, 1953). This year, 1951, was chosen because it is the latest in

TABLE II

LEGITIMATE MATERNITIES, BY BIRTH ORDER

England and Wales, Northern Region, 1951

| Birth Order | Number of Babies |
|---|---|
| 1 | 18,787 |
| 2 | 15,685 |
| 3 | 8,548 |
| 4 | 4,163 |
| 5 | 2,220 |
| 6 | 1,152 |
| 7 | 671 |
| 8 | 410 |
| 9 | 285 |
| 10 | 178 |
| 11+ | 212 |
| Total | 52,311 |

which the Registrar-General gave regional data, and because, judging from the national figures from 1947, it seems reasonably representative of the period as a whole. The secular changes of birth order distribution during the period 1947 to 1956 are relatively small when we ignore, as we do in computing the distributions, the proportion of first births, and when we need to know only the proportion of second to third and later births. The "Northern Region" is greater than the area we have covered, but in the years up to 1949, when figures for North I (Northumberland and Durham) and the Northern Region (Northumberland, Durham, Cumberland, Westmorland and North Riding of Yorkshire) were published together, the birth order differences between the two were trivial. Like the Registrar-General, we have included both live and stillbirths in assessing birth order; the only difference is that he limits his data to legitimate maternities.

TABLE III

PROPORTIONATE DISTRIBUTIONS, ACCORDING TO BIRTH ORDER, OF "FIRST AFFECTED" BABIES

Values expected at different levels of probability of sensitization ($p$)

| Birth Order | $p$ | | | | Observed |
|---|---|---|---|---|---|
| | Very Small | 0·05 | 0·1 | 0·2 | |
| 2 | 43·3 | 44·9 | 47·0 | 51·0 | 43·4 |
| 3 | 25·5 | 26·6 | 26·7 | 26·6 | 28·9 |
| 4 | 13·7 | 13·2 | 12·7 | 11·7 | 13·4 |
| 5 | 7·5 | 6·9 | 6·5 | 5·5 | 8·2 |
| 6+7 | 6·3 | 5·5 | 4·8 | 3·7 | 3·7 |
| 8 or Later | 3·8 | 3·0 | 2·3 | 1·5 | 2·5 |
| Total | 100·1 | 100·1 | 100·0 | 100·0 | 100·1 |
| $\chi^2$ | 18·0 | 10·5 | 11·4 | 31·7 | — |

*Note:* $\chi^2$ is estimated by the application of the calculated proportions to 904 children and comparision with the observed distribution.

It is clear from Table III that only the distributions in the region of $p = 0{\cdot}05$ are compatible with the observed distribution. This estimate refers only to the susceptible part of the population. In the whole population of this district, we know the incidence of haemolytic disease of the newborn to be about 5 per thousand births, and in our experience 64 per cent. of these (3·2 per 1,000 births) are "first affected" babies. Of every thousand births, 140 are to the D-negative wives of D-negative husbands. When we applied the calculated risks of babies being "first affected" to 140 babies distributed as in Table II, we found that the observed incidence of 3·2 per 1,000 births was best matched upon the supposition that $p = 0{\cdot}06$.

This estimate of $p$ in the whole population of D-negative mothers is no less than our estimate of $p$ in the susceptible part of this population. If the terms of our model are accepted, it follows that all, or almost all, D-negative women, are susceptible.

*The Validity of the Model.*—This conclusion is conditional upon the validity of our model and we must therefore reconsider its premises. We presumed, in constructing it, that $p$ was constant throughout the susceptible population, but we know that this is not strictly so. The probability of sensitization is influenced, for example, by the ABO compatibility of mother and foetus (Mollison, Mourant, and Race, 1952), and it has been shown that $R_2$ is a more powerful antigen than $R_1$ (Murray, 1957). A large proportion of these effects is randomly determined after marriage, but, part at least, is predetermined. If, however, the distribution of $p$ is wider than we have presumed, this can only strengthen our general conclusion, for over-representation of mothers in the upper part of its range must have moved the observed distribution of births to the left. Indeed, the tolerance between the observed distribution and that for the lowest possible values of $p$ is so narrow as to suggest that the range of $p$ must be within close limits.

We also presumed, in constructing the model, that $p$ operated at the sensitization level, and that, once sensitized, a mother would always become immunized to the next Rh-positive child; but there are at least two other possibilities.

The first is the converse of our model, namely that initial sensitization is universal and subsequent immunization proportional. This could occur, for example, if the necessary correspondence between successive babies were not simply that they should both be Rh-positive, but that they should correspond exactly in some combination of several (unknown) factors.

The second main possibility is that both initial sensitization and subsequent immunization depend upon proportional risks. This, for example, would be the situation if the accidental release of foetal blood into the maternal circulation were necessary in each of two pregnancies. In this example, both risks might be nearly equal.

At the cost of increased complexity, we may extend the generality of our model to cover both of these possibilities, as well as the original one. This is done by resolving $p$ into two values: a probability of sensitization ($s$) at an early pregnancy, and a probability of immunization to an effective level ($t$) at a

later one. It is specified therefore that $st$ equals $p$ as used in the original model.

The probability that a baby of given birth order will be a "first affected" baby is calculable, for homozygous fathers, as follows:

Pregnancy 1 . . . 0
Pregnancy 2 . . . $st$
Pregnancy 3 . . . $st[(1-s)+(1-t)]$
Pregnancy 4 . . . $st[(1-s)^2+(1-s)(1-t)+(1-t)^2]$
Pregnancy 5 . . . $st[(1-s)^3+(1-s)^2(1-t)+(1-s)(1-t)^2+(1-t)^3]$
Pregnancy 6 . . . $st[(1-s)^4+(1-s)^3(1-t)+(1-s)^2(1-t)^2+(1-s)(1-t)^3+(1-t)^4]$
Pregnancy $n$ . . . $st[(1-s)^{n-2}(1-t)^0+(1-s)^{n-3}(1-t)^1 \ldots\ldots+(1-s)^0(1-t)^{n-2}]$.

For heterozygous fathers the sequence is similar, but $s$ is replaced by $\frac{s}{2}$, and $t$ by $\frac{t}{2}$:

Pregnancy 1 . . . 0
Pregnancy 2 . . . $\frac{st}{4}$
Pregnancy 3 . . . $\frac{st}{4}\left[\left(1-\frac{s}{2}\right)+\left(1-\frac{t}{2}\right)\right]$ . . . etc.

It is simply shown that, as $t$ approaches 1 (and $s$ approaches the $p$ of the original model), these expressions approximate to those we have already used. It is clear also, from the symmetry of the above terms, that the expressions derived for our original model cover also the first alternative possibility, namely that of universal sensitization and proportional immunization; the effect of $s$ approaching 1 is the same as the effect of $t$ approaching 1. It remains only to consider, then, the supposition that both $s$ and $t$ are proportional.

The greatest departure from the original model occurs when $s$ equals $t$. This is also the likely consequence of the specific example (*i.e.* two leakages of foetal blood) which we quoted. In this event, the general model for homozygous fathers reduces to:

Pregnancy 1 . . . 0
Pregnancy 2 . . . $p$
Pregnancy 3 . . . $2p(1-\sqrt{p})$
Pregnancy 4 . . . $3p(1-\sqrt{p})^2$
Pregnancy 5 . . . $4p(1-\sqrt{p})^3$
Pregnancy $n$ . . . $(n-1)p(1-\sqrt{p})^{n-2}$ . . where $p=st$.

For heterozygotes, $p$ is replaced by $\frac{p}{4}$, thus:

Pregnancy 2 . . . $\frac{p}{4}$
Pregnancy 3 . . . $\frac{2p}{4}\left(1-\sqrt{\frac{p}{4}}\right)$
Pregnancy 4 . . . $\frac{3p}{4}\left(1-\sqrt{\frac{p}{4}}\right)^2$
Pregnancy $n$ . . . $\frac{(n-1)p}{4}\left(1-\sqrt{\frac{p}{4}}\right)^{n-2}$.

These values differ considerably from those of our earlier hypotheses and we have therefore recalculated the expected distributions for various values of $p$ (*i.e.* $st$). These are compared with the observed data in Table IV.

TABLE IV

PROPORTIONATE DISTRIBUTIONS, ACCORDING TO BIRTH ORDER, OF "FIRST AFFECTED" BABIES

Values expected when the probability of sensitization ($s$) and immunization ($t$) are equal, at different levels of their product ($p$)

| Birth Order | $p$ | | | | Observed |
|---|---|---|---|---|---|
| | 0·05 | 0·1 | 0·15 | 0·2 | |
| 2 | 32·5 | 37·6 | 41·5 | 44·5 | 43·4 |
| 3 | 28·6 | 29·7 | 29·9 | 29·6 | 28·9 |
| 4 | 16·9 | 15·9 | 14·7 | 13·6 | 13·4 |
| 5 | 9·7 | 8·3 | 7·2 | 6·2 | 8·2 |
| 6+7 | 8·1 | 6·1 | 4·9 | 4·8 | 3·7 |
| 8 or Later | 4·2 | 2·3 | 1·8 | 1·4 | 2·5 |
| Total | 100·0 | 99·9 | 100·0 | 100·1 | 100·1 |
| $\chi^2$ | 69·2 | 21·3 | 8·8 | 18·4 | — |

The best fit upon this hypothesis is when $p$ is approximately 0·15, that is, $s=t=0·39$. This value, if applied to all relevant marriages, would give an incidence of 8·6 "first affected" infants per thousand births, compared with the observed incidence of 3·2 per 1,000 births. But if only 37 per cent. of D-negative women were susceptible, we could postulate that two events, each with a probability of 0·39 and occurring at two separate pregnancies, were necessary for the development of immunity.

This then is a second and alternative explanation of the facts.

## DISCUSSION

Our conclusions take the form of two main alternatives.

1 (*a*) The ability to develop Rh antibodies is not

predetermined, and any Rh-negative woman may produce them.

(*b*) Whether or not immunity develops is determined after marriage, and the process is triggered by a single event, the risk of whose occurrence is about 1:17. This is probably related to one of the pregnancies, but our method does not distinguish which pregnancy this is.

2 (*a*) The ability to develop Rh antibodies is predetermined and only a proportion of women can produce them.

(*b*) In the susceptible women, the process is triggered by a series of two events in different pregnancies.

(*c*) If we presume that the two events have an equal probability of occurrence, the risk of each is about 0·39, and the proportion of D-negative women who are susceptible is about 37 per cent.

These alternatives represent only the limits of a continuous series of possibilities where, beginning at the second hypothesis, the proportion of susceptible women rises as the probabilities of the two events become unequal in either direction, and the first hypothesis constitutes the limit.

The fact that both universal susceptibility and the elimination of one of the two events occur at the same point on this scale adds to the plausibility of the first hypothesis. But the ultimate distinction between the two alternatives will rest upon other data. Unfortunately, those so far published seem contradictory. Gerrard and Waterhouse (1953) studied the sisters of immunized women, but found no evidence of the genetic determinants postulated by Wiener (1946). Owen, Wood, Foord, Sturgeon, and Baldwin (1954) produced data in support of their ingenious suggestion of a predetermining factor based upon immunological tolerance, but the data of Booth, Dunsford, Grant, and Murray (1953) seem incompatible. Nevanlinna (1953), who, like ourselves, studied the birth order distribution, supported Wiener's genetic hypothesis. This was because of a relatively increased proportion of early births in his data, a difference for which we have no explanation.

Our first approach to this problem has also resolved itself into a paradox. On the one hand it is plain that we have failed to exclude the possibility of predetermined susceptibility, but on the other hand universal susceptibility is seen to be possible, and failure of immunization at early pregnancies is therefore no reassurance for later ones.

## Summary

The nature of the determinants of Rhesus isoimmunization must affect the birth order distribution of "first affected" babies, and the expected values are calculated upon a series of hypotheses.

The observed values correspond with one or other of two main hypotheses. The first supposes that all women are susceptible and that the main determinant is a single event, occuring after marriage, and that the risk of this event is about one in seventeen. The second supposes that only a proportion of women are susceptible and that for them the disease is determined by two events in different pregnancies, each with a relatively high risk of occurrence.

In either event, failure to develop antibodies in early pregnancies is no reassurance for later ones.

We should like to thank David Newell for his advice and constructive criticism.

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# SOME ASPECTS OF GROWTH WITH NORMS FROM BIRTH TO 18 YEARS

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Several cross-sectional studies of children's body measurements have been made from which average growth may be inferred (Hammond, 1953a; Provis and Ellis, 1955; Clements and Pickett, 1955 and 1956 for school ages. Low, 1952; Acheson and Hewitt, 1954; Hammond, 1955; Thomson, 1956 for pre-school ages). But it is impossible to assess the significance of departures from average growth unless normal growth variability is known, and this can be ascertained only from actual differences shown by individuals between successive measuring occasions.

Usually growth is studied over one year, but its consistency over longer periods can be assessed by comparing successive years' growth with each other and with that of the longer periods. The data used in this paper, collected from a number of different studies, are based on growth measurements taken over intervals of 1 to 3 years from birth to late adolescence. They consist of measurements of growth taken by the author in the following investigations:

(1) A pilot survey of infants' growth from birth to 5 years (Hammond, 1955);

(2) A Ministry of Health survey of the growth and development of children of different socio-economic levels aged 5 to 18 years (Hammond, 1953b);

(3) Growth records taken at Camp Schools (unpublished Ph.D. thesis; University of London);

(4) A growth survey at the National Children's Home, Harpenden (unpublished);

(5) A nutritional survey at Rotherham (in the press).

## Measuring Errors

Growth represents the difference between two measurements and it is therefore subject to the ordinary errors of measurement on either occasion; hence standard deviations of errors of growth tend to be $\sqrt{2}$ times those of single measurements. Constant errors (*e.g.* in instruments or technique) which apply to both measuring occasions, leave the mean growth and its variability unaffected. Random errors increase the variability of growth rather than its mean but, more important, they affect two adjacent years' growth in opposite ways, tending to produce apparent inconsistency in growth. As the total coefficients of variation of growth are high and the error variance seldom exceeds 5 per cent. of the growth variance for any year, no allowance for errors has been made either to the means or to the correlations reported later.

## Age and Growth Patterns

For the purpose of providing growth norms, children considered to be suffering from clinical abnormality or malnutrition have been excluded from Tables I and II (overleaf) and Figs 1 and 2 (overleaf). For both weight and height, the annual increment is greatest in the first year of life. Thereafter the weight increment remains fairly constant until about the fifth year and then gradually increases until the pubertal spurt is reached. The annual height increment, on the other hand, decreases until the fifth year and then remains fairly constant until the pubertal spurt. This pattern, of course, is fairly well known from cross-sectional studies.

It is perhaps not generally realized that, on average, weight and height growth during the first year of life are—even in absolute amounts—greater than during any other year. When expressed as a proportion of the attained measurements, growth during the first years is relatively greater, and the pattern is then one of progressive decrease, arrested temporarily by the pubertal spurt.

Development occurs at different rates in individuals, and growth should be compared with the

TABLE I

WEIGHT GROWTH OVER 1, 2, AND 3 YEARS, BY SEX

| Initial Age (yrs) | Sex | 1 Year | | | 2 Years | | | 3 Years | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. |
| Birth | Boys | 214 | 6·89 | 1·00 | 326 | 9·71 | 1·77 | 204 | 11·38 | 1·68 |
| | Girls | 237 | 6·62 | 1·27 | 290 | 10·70 | 1·22 | 205 | 12·29 | 2·00 |
| 1 | Boys | 44 | 2·04 | 0·54 | 34 | 4·58 | 0·73 | 41 | 6·30 | 1·18 |
| | Girls | 45 | 2·00 | 0·64 | 34 | 4·58 | 0·73 | 41 | 6·30 | 1·18 |
| 2 | Boys | 24 | 1·72 | 0·45 | 36 | 3·76 | 0·91 | 35 | 5·40 | 1·27 |
| | Girls | 34 | 2·18 | 0·54 | 33 | 4·04 | 0·64 | 31 | 6·03 | 0·86 |
| 3 | Boys | 27 | 2·00 | 1·04 | 19 | 3·13 | 1·68 | — | — | — |
| | Girls | 37 | 2·09 | 0·64 | 33 | 3·95 | 0·67 | — | — | — |
| 4 | Boys | 38 | 1·72 | 0·91 | 7 | 4·35 | 1·36 | — | — | — |
| | Girls | 41 | 2·00 | 0·77 | (2) | 2·86 | — | — | — | — |
| 5 | Boys | 59 | 2·04 | 1·00 | 6 | 4·35 | 1·86 | 29 | 6·03 | 1·68 |
| | Girls | 46 | 2·14 | 0·86 | 11 | 4·94 | 0·91 | 46 | 6·49 | 1·32 |
| 6 | Boys | 51 | 2·18 | 1·04 | (3) | 4·72 | — | 34 | 6·94 | 2·18 |
| | Girls | 55 | 2·49 | 0·86 | 15 | 4·72 | 0·77 | 41 | 6·21 | 1·54 |
| 7 | Boys | 57 | 2·31 | 0·82 | 7 | 4·35 | 0·96 | 35 | 7·03 | 1·68 |
| | Girls | 69 | 2·45 | 1·19 | 28 | 5·49 | 1·59 | 55 | 7·48 | 2·40 |
| 8 | Boys | 79 | 2·54 | 1·27 | 20 | 5·81 | 1·90 | 62 | 8·48 | 2·13 |
| | Girls | 96 | 2·86 | 1·27 | 30 | 7·48 | 3·72 | 84 | 7·71 | 3·36 |
| 9 | Boys | 109 | 2·63 | 1·09 | 42 | 6·03 | 2·13 | 95 | 9·39 | 2·99 |
| | Girls | 93 | 2·81 | 1·40 | 21 | 7·85 | 4·17 | 70 | 9·57 | 3·90 |
| 10 | Boys | 99 | 3·04 | 1·27 | 68 | 7·85 | 1·95 | 46 | 10·34 | 3·45 |
| | Girls | 84 | 3·72 | 1·73 | 25 | 9·30 | 4·22 | 67 | 11·88 | 3·76 |
| 11 | Boys | 96 | 3·49 | 1·73 | 28 | 8·71 | 2·40 | 34 | 13·38 | 4·67 |
| | Girls | 88 | 4·49 | 2·00 | 24 | 11·15 | 3·45 | 76 | 13·74 | 3·67 |
| 12 | Boys | 69 | 4·58 | 2·82 | 19 | 10·39 | 2·99 | 33 | 12·97 | 4·17 |
| | Girls | 80 | 5·03 | 1·84 | 31 | 11·43 | 2·72 | 34 | 12·34 | 3·63 |
| 13 | Boys | 41 | 5·35 | 2·54 | 11 | 12·24 | 4·35 | 43 | 13·74 | 4·76 |
| | Girls | 70 | 4·86 | 2·18 | 6 | 8·21 | 4·13 | 46 | 10·84 | 3·63 |
| 14 | Boys | 55 | 5·81 | 2·40 | (3) | 8·39 | — | 44 | 10·44 | 5·26 |
| | Girls | 66 | 2·86 | 2·00 | — | — | — | 49 | 6·80 | 4·85 |
| 15 | Boys | 51 | 4·63 | 2·99 | (3) | 8·35 | — | 10 | 10·25 | 3·45 |
| | Girls | 43 | 2·27 | 1·72 | — | — | — | — | — | — |
| 16 | Boys | 51 | 3·08 | 2·31 | — | — | — | — | — | — |
| | Girls | 30 | 0·27 | 1·22 | — | — | — | — | — | — |
| 17 | Boys | 28 | 2·86 | 2·09 | (2) | 4·54 | — | — | — | — |
| | Girls | — | — | — | — | — | — | — | — | — |

TABLE II

HEIGHT GROWTH OVER 1, 2, AND 3 YEARS

| Initial Age (yrs) | Sex | 1 year | | | 2 years | | | 3 years | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | Mean (cm.) | s.d. | No. | Mean (cm.) | s.d. | No. | Mean (cm.) | s.d. |
| Birth | Boys | 214 | 24·8 | 2·5 | 42 | 33·3 | 3·8 | 23 | 42·6 | 3·9 |
| | Girls | 237 | 24·2 | 2·4 | 37 | 33·6 | 2·1 | 32 | 43·9 | 2·6 |
| 1 | Boys | 44 | 11·0 | 1·7 | 24 | 22·7 | 2·3 | 34 | 29·5 | 2·3 |
| | Girls | 45 | 11·7 | 1·8 | 35 | 22·1 | 2·5 | 41 | 30·5 | 2·7 |
| 2 | Boys | 23 | 9·3 | 1·3 | 33 | 15·8 | 1·3 | 37 | 22·1 | 1·9 |
| | Girls | 34 | 10·3 | 0·8 | 34 | 16·0 | 1·6 | 32 | 22·2 | 2·2 |
| 3 | Boys | 21 | 7·4 | 1·3 | 23 | 13·3 | 1·9 | — | — | — |
| | Girls | 31 | 7·6 | 1·2 | 33 | 13·7 | 1·4 | — | — | — |
| 4 | Boys | 24 | 3·7 | 1·9 | — | — | — | — | — | — |
| | Girls | 26 | 4·3 | 0·9 | — | — | — | — | — | — |
| 5 | Boys | 45 | 6·1 | 1·3 | — | — | — | 29 | 17·9 | 2·3 |
| | Girls | 45 | 5·6 | 1·1 | 7 | 11·6 | 1·1 | 39 | 16·4 | 2·7 |
| 6 | Boys | 42 | 5·3 | 1·3 | — | — | — | 34 | 17·0 | 2·4 |
| | Girls | 55 | 5·3 | 1·5 | 9 | 11·2 | 1·6 | 32 | 16·4 | 1·8 |
| 7 | Boys | 71 | 5·7 | 1·0 | 7 | 10·7 | 1·4 | 41 | 15·7 | 1·8 |
| | Girls | 72 | 4·6 | 1·0 | 6 | 11·2 | 2·5 | 39 | 15·7 | 2·3 |
| 8 | Boys | 100 | 5·0 | 0·9 | 22 | 10·2 | 1·6 | 62 | 15·0 | 2·0 |
| | Girls | 116 | 4·7 | 1·0 | 19 | 11·8 | 2·8 | 43 | 16·2 | 2·0 |
| 9 | Boys | 144 | 4·6 | 1·2 | 19 | 9·1 | 2·2 | 93 | 14·4 | 2·2 |
| | Girls | 125 | 4·8 | 1·4 | 21 | 12·2 | 2·4 | 40 | 16·4 | 3·4 |
| 10 | Boys | 123 | 4·5 | 1·1 | 16 | 10·6 | 2·9 | 37 | 14·9 | 2·9 |
| | Girls | 123 | 5·3 | 2·1 | 53 | 13·8 | 2·9 | 42 | 18·2 | 3·6 |
| 11 | Boys | 118 | 5·0 | 1·8 | 14 | 12·3 | 3·2 | 27 | 17·3 | 4·0 |
| | Girls | 124 | 5·8 | 2·2 | 58 | 13·2 | 2·5 | 54 | 15·6 | 3·6 |
| 12 | Boys | 80 | 6·8 | 2·4 | 17 | 12·5 | 3·2 | 18 | 18·6 | 4·3 |
| | Girls | 117 | 5·4 | 2·0 | 56 | 10·8 | 2·7 | (3) | 14·7 | — |
| 13 | Boys | 70 | 6·6 | 2·5 | 9 | 13·7 | 2·9 | (1) | 17·0 | — |
| | Girls | 96 | 4·1 | 1·8 | 51 | 6·9 | 3·9 | — | — | — |
| 14 | Boys | 69 | 5·8 | 2·3 | 46 | 12·9 | 4·0 | — | — | — |
| | Girls | 65 | 2·1 | 1·3 | 50 | 3·9 | 3·3 | — | — | — |
| 15 | Boys | 46 | 5·0 | 3·0 | — | — | — | — | — | — |
| | Girls | 45 | 1·6 | 1·2 | — | — | — | — | — | — |
| 16 | Boys | 44 | 2·3 | 1·9 | — | — | — | — | — | — |
| | Girls | 31 | 0·4 | 0·6 | — | — | — | — | — | — |
| 17 | Boys | 24 | 1·8 | 1·7 | — | — | — | — | — | — |
| | Girls | — | — | — | — | — | — | — | — | — |

appropriate maturity level rather than with the chronologically equivalent age, especially around puberty. At this age the mean growth is affected by the accelerated growth during puberty of the earliest maturer and continues to be affected until the latest maturer has finished his spurt; hence standard deviations are high and the pattern of the means is flattened and may not be followed by any individual. Nevertheless the mean will reflect the proportion who have actually reached their spurt at the different ages. The relation between growth and puberty is sufficiently well defined to indicate whether or not a growth spurt should be expected in any individual. After age 10 the expected growth will be nearer 3 kg. and 4–5 cm. per year for pre-pubescent children and 6–7 kg. and 8–10 cm. per year for children showing physical signs of puberty. Similarly, children maturing early who have already passed their peak spurt will be expected to gain an amount more nearly equal to the post-pubescent growth levels of 2·2 kg. and 2·5 cm. or less. These figures are intended only for guidance where the stage of puberty is not known with certainty, *e.g.* as in school records.

Growth over a 2- or 3-year interval will include children who are passing through the various stages of puberty and the effect is to spread the peak growth still further.

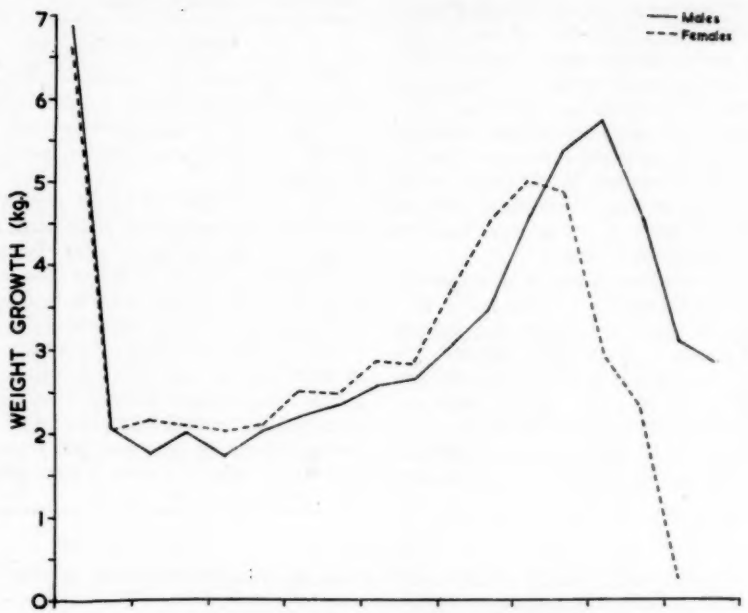


FIG. 1.—Weight growth from birth to 18 years in boys and girls.

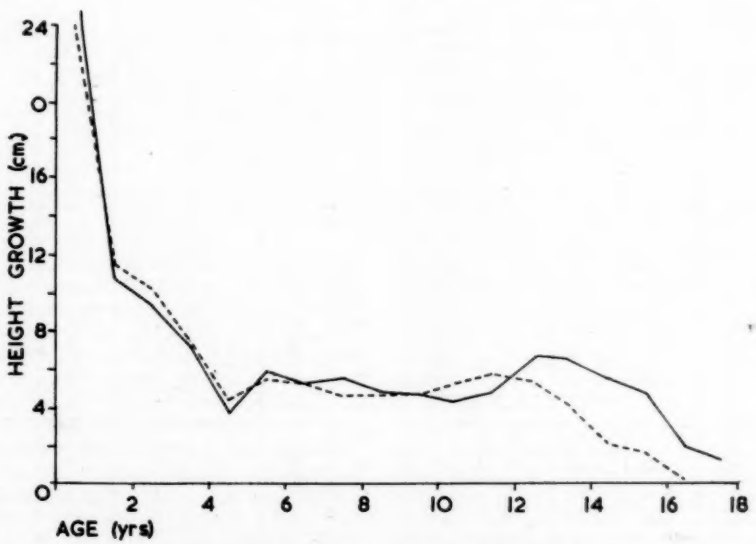


FIG. 2.—Height growth from birth to 18 years in boys and girls.

### Age and Growth Variability

The variability of weight growth follows a somewhat different pattern from that of the average growth with age, especially during infancy. For example, the average yearly weight growth decreases from approximately six times its standard deviation during the first year to twice the standard deviation during the pubertal years and little more than its standard deviation thereafter. Height growth is less variable and decreases from about seven times its standard deviation up to age 3 to three times its standard deviation around puberty.

The standard deviations of growth in weight and height for two-year intervals are higher for boys than for girls up to ages 5 or 6. From then until age 11 or 12, the growth of girls is more variable. The sex difference in variability is due to the different times at which maximum growth occurs in boys and girls. Three-year growth increases maintain a more constant level relative to their variability at different ages. (In this respect weight growth over three years is about comparable with height growth over one year.)

### Socio-Economic Class

The socio-economic status of the child was assessed from the parents' circumstances (occupation and way of living) in Investigations 1, 3, and 5, and as a group characteristic (type of school) in Investigation 2.

The mean weight and height growth of two extreme social groups (mainly professional or executive groups at fee-paying schools compared with working-class children living in slum districts) are shown in Table III and in Table IV (opposite).

Weight growth in the better social group (Group A) exceeds that in Social Group B for boys and girls at nearly all ages, and there is a suggestion that, for girls at least, pubertal growth reaches its peak later and continues later in Social Group B. The annual height increase for boys and girls is clearly greater in Group A than in Group B until late puberty.

Table III

MEAN YEARLY WEIGHT GAINS IN TWO SOCIAL GROUPS, BY SEX

| Sex .. | Boys | | | | | | Girls | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Social Group | A | | | B | | | A | | | B | | |
| Age (yrs) | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. |
| 0–1 | 19 | 7·26 | 1·37 | 195 | 6·99 | 1·00 | 26 | 6·49 | 1·45 | 209 | 6·62 | 1·00 |
| 1–2 | — | — | — | 44 | 2·04 | 0·54 | — | — | — | 45 | 2·00 | 0·64 |
| 2–3 | — | — | — | 24 | 1·72 | 0·45 | — | — | — | 34 | 2·18 | 0·54 |
| 3–4 | — | — | — | 27 | 2·00 | 1·04 | — | — | — | 37 | 2·09 | 0·63 |
| 4–5 | — | — | — | 36 | 1·68 | 0·86 | — | — | — | 41 | 1·72 | 0·91 |
| 5–6 | 10 | 1·68 | 1·00 | 49 | 2·27 | 1·00 | 9 | 2·54 | 0·82 | 41 | 1·86 | 0·86 |
| 6–7 | 7 | (2·1) | 1·13 | 47 | 2·18 | 0·64 | 13 | 2·86 | 0·73 | 45 | 2·09 | 0·91 |
| 7–8 | 7 | (2·4) | 0·54 | 58 | 2·31 | 0·95 | 32 | 2·86 | 1·32 | 43 | 2·18 | 0·73 |
| 8–9 | 31 | 2·54 | 1·27 | 74 | 2·49 | 1·04 | 48 | 3·27 | 1·09 | 72 | 2·40 | 1·27 |
| 9–10 | 57 | 2·86 | 1·22 | 91 | 2·49 | 1·00 | 36 | 2·95 | 1·41 | 90 | 2·77 | 1·18 |
| 10–11 | 64 | 3·22 | 1·32 | 78 | 2·86 | 1·09 | 49 | 4·17 | 1·86 | 75 | 3·58 | 1·90 |
| 11–12 | 73 | 3·58 | 1·95 | 74 | 3·40 | 1·50 | 39 | 4·54 | 1·86 | 98 | 4·49 | 2·22 |
| 12–13 | 19 | 4·98 | 2·99 | 94 | 4·08 | 2·90 | 40 | 4·67 | 1·59 | 96 | 5·17 | 1·72 |
| 13–14 | 38 | 5·44 | 2·59 | 49 | 5·31 | 2·00 | 67 | 3·76 | 2·09 | 56 | 5·22 | 2·18 |
| 14–15 | 55 | 5·58 | 2·40 | 22 | 5·54 | 3·45 | 60 | 2·63 | 1·77 | 14 | 3·49 | 2·00 |
| 15–16 | 53 | 4·85 | 2·95 | 10 | (3·4) | 1·81 | 43 | 2·27 | 1·72 | — | — | — |
| 16–17 | 44 | 2·99 | 2·31 | 7 | (3·7) | 1·59 | 31 | 0·27 | 0·77 | — | — | — |
| 17–18 | 24 | 2·86 | 2·22 | 3 | (2·8) | — | — | — | — | — | — | — |

TABLE IV
MEAN YEARLY HEIGHT GAINS IN TWO SOCIAL GROUPS, BY SEX

| Sex .. | Boys | | | | | | Girls | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Social Group | A | | | B | | | A | | | B | | |
| Age (yrs) | No. | Mean (cm.) | s.d. | No. | Mean (cm.) | s.d. | No. | Mean (cm.) | s.d. | No. | Mean (cm.) | s.d. |
| 5 | 10 | 6·40 | — | 33 | 5·86 | 1·35 | 9 | 5·61 | 1·51 | 37 | 5·56 | 1·07 |
| 6 | 7 | (5·47) | — | 33 | 5·20 | 1·32 | 13 | 5·28 | 0·90 | 42 | 5·30 | 1·54 |
| 7 | 7 | (6·32) | — | 50 | 5·11 | 1·03 | 34 | 5·07 | 1·29 | 41 | 4·24 | 1·40 |
| 8 | 31 | 5·22 | 0·90 | 69 | 4·78 | 0·93 | 45 | 5·70 | 1·29 | 71 | 3·97 | 1·00 |
| 9 | 57 | 5·46 | 1·17 | 97 | 4·00 | 0·82 | 37 | 5·50 | 1·27 | 87 | 4·27 | 1·38 |
| 10 | 64 | 5·19 | 1·07 | 80 | 4·20 | 0·84 | 48 | 6·18 | 1·48 | 73 | 4·90 | 2·12 |
| 11 | 73 | 5·42 | 1·76 | 68 | 4·80 | 1·00 | 37 | 6·19 | 1·57 | 80 | 5·55 | 2·20 |
| 12 | 19 | 5·09 | 2·44 | 82 | 4·50 | 2·48 | 41 | 5·05 | 1·96 | 79 | 5·63 | 1·96 |
| 13 | 38 | 5·71 | 2·50 | 49 | 6·24 | 2·42 | 70 | 3·80 | 1·85 | 30 | 4·21 | 2·02 |
| 14 | 55 | 5·60 | 2·32 | 16 | 7·61 | — | 49 | 1·62 | 1·31 | 5 | (3·1) | — |
| 15 | 53 | 4·88 | 2·98 | 2 | (7·6) | — | 43 | 1·34 | 1·22 | 2 | (3·0) | — |
| 16 | 44 | 2·30 | 1·89 | — | — | — | 30 | 0·37 | 0·59 | — | — | — |
| 17 | 24 | 1·83 | 1·75 | — | — | — | — | — | — | — | — | — |

## HEALTH STATUS

Health experience was assessed at the time of measuring.

In the Infant Growth Survey (Investigation 1) the following mean weight gains were made from birth to one year:

| Health Experience | Boys | | | Girls | | |
|---|---|---|---|---|---|---|
| | No. | Mean (kg.) | s.d. | No. | Mean (kg.) | s.d. |
| No Illness .. .. | 84 | 7·03 ± | ·12 | 101 | 6·55 ± | ·10 |
| Cold or Slight Illness | 68 | 6·55 ± | ·14 | 95 | 6·38 ± | ·10 |
| Longer or More Serious Illness | 33 | 6·78 ± | ·19 | 19 | 6·32 ± | ·23 |

For children of low nutritional grade (Investigation 2) the results were as follows:

33 children were marked down clinically at the first and second assessments; of these 25 gained less than the average weight during the year. Out of 64 who were marked down at the first assessment but were normal at the second assessment, 32 still failed to make the average weight gain. In addition, 43 children were marked "normal" at the first examination and were down-graded at the second; of these, 35 failed to put on the average increase of weight. That is to say, the children initially down-graded gained less weight in the following year than did the normal children (unless they reached the normal standard, in which case they tended to gain as much weight as the normal group), whilst children whose clinical status went down from first to second assessment put on even less weight.

The Rotherham Group Study (Investigation 5) included three groups of children aged 7 to 15 years:

(1) Children suffering from general nutritional debility attending an open-air school (nutritional group);

(2) Their brothers and sisters not requiring special treatment (sibling group);

(3) A control group of similar ages attending ordinary day schools.

Weight and height gains over the 3 years of the study are shown in Table V (overleaf).

During the first year the nutritional group gained least weight (less than the average L.C.C. child of comparable age (Scott, 1955), and considerably less than the control group). After the first year the nutritional group gained more weight than their brothers and sisters, and their height gain was greater than for the controls and was also above L.C.C. standards.

Home conditions were least good for the nutritional group children and their siblings, but during school hours conditions were most favourable for the nutritional group, and least favourable for their siblings. The results are dealt with more fully in another publication (Gillett and Hammond, in the press).

TABLE V

GAIN IN WEIGHT AND HEIGHT ACCORDING TO NUTRITIONAL CATEGORY

| Year | 1951–2 | | | | | 1952–3 | | | | | 1953–4 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gain | Weight (kg.) | | | Height (cm.) | | Weight (kg.) | | | Height (cm.) | | Weight (kg.) | | | Height (cm.) | |
| | No. | Mean | s.d. | Mean | s.d. | No. | Mean | s.d. | Mean | s.d. | No. | Mean | s.d. | Mean | s.d. |
| Nutritional Group | 154 | 2·86 | 1·27 | 5·4 | 1·4 | 85 | 3·63 | 1·45 | 5·9 | 1·8 | 73 | 3·99 | 1·59 | 5·7 | 2·1 |
| Sibling Group | 46 | 3·27 | 1·72 | 5·2 | 1·8 | 21 | 2·86 | 1·81 | 4·5 | 1·6 | 13 | 3·93 | 1·81 | 5·7 | 1·7 |
| Control Group | 95 | 3·89 | 1·76 | 5·8 | 1·5 | 46 | 4·72 | 2·03 | 6·1 | 1·9 | 43 | 4·90 | 3·13 | 5·0 | 1·9 |
| L.C.C. Mean Differences | — | 3·67 | — | 5·4 | — | — | 3·86 | — | 5·3 | — | — | 4·00 | — | 5·5 | — |

For groups, weight and height growth shows differences consistent with their nutritional grading, as we should expect; but, for individuals, growth variability is so high that growth can only be used as an indication of nutritional condition in conjunction with other criteria.

## PHYSICAL TYPE

During infancy the growth of two physical types—leptosomes (long, thin), and eurysomes (short, broad)—was studied in relation to type constancy (Hammond, 1957). Leptosomes were found to gain *more* weight relative to height than eurysomes.

For schoolchildren (Investigation 2) two types consisting of leptosomes and pyknics (short, fat, rounded type) were differentiated on the basis of twenty physical measurements. The mean annual weight growth of these types is shown in Table VI*

* In all cases the types were first differentiated and subsequent growth compared. Studies in which past growth of physical types is compared involve a circular reasoning, since leptosome types, for example, are just those children whose weight is low relative to height and in whom therefore weight growth has necessarily not kept pace with height growth.

TABLE VI

ANNUAL WEIGHT AND HEIGHT GAIN ACCORDING TO PHYSICAL TYPE

| Gain | Weight (kg.) | | | | | | | | Height (cm.) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | Boys | | | | Girls | | | | Boys | | Girls | |
| Type | Leptosome | | Pyknic | | Leptosome | | Pyknic | | Leptosome | Pyknic | Leptosome | Pyknic |
| Age (yrs) | No. | kg. | No. | kg. | No. | kg. | No. | kg. | (cm.) | (cm.) | (cm.) | (cm.) |
| Birth | 31 | 7·47 | 22 | 6·31 | 26 | 7·09 | 42 | 6·52 | 22·60 | 20·62 | 22·14 | 20·88 |
| 1 | 22 | 2·54 | 21 | 2·30 | 24 | 2·47 | 17 | 2·47 | 13·75 | 13·40 | 13·85 | |
| 2 | 9 | 1·97 | 8 | 1·80 | 20 | 2·03 | 5 | (1·90) | 8·60 | 8·68 | 8·59 | (8·82) |
| 3 | 10 | 2·09 | 7 | (1·28) | 15 | 1·78 | 16 | 2·12 | 6·84 | 7·00 | 7·42 | 7·59 |
| 4 | 11 | 1·51 | 13 | 1·81 | 12 | 1·99 | 13 | 2·00 | 6·32 | 6·10 | 6·09 | 6·34 |
| 5 | 23 | 1·77 | 14 | 1·91 | 24 | 2·17 | 22 | 2·15 | 5·94 | 5·70 | 5·93 | 5·28 |
| 6 | 21 | 2·04 | 16 | 1·70 | 27 | 2·53 | 28 | 2·02 | 5·12 | 5·42 | 5·33 | 4·97 |
| 7 | 25 | 2·38 | 23 | 2·11 | 37 | 2·47 | 32 | 2·45 | 5·30 | 5·79 | 4·63 | 4·56 |
| 8 | 41 | 2·40 | 38 | 2·45 | 50 | 2·93 | 46 | 2·74 | 4·79 | 4·60 | 4·70 | 4·57 |
| 9 | 54 | 2·52 | 55 | 2·65 | 48 | 2·64 | 45 | 2·80 | 4·93 | 4·29 | 4·68 | 4·42 |
| 10 | 48 | 2·95 | 51 | 2·65 | 42 | 3·53 | 42 | 3·94 | 5·84 | 4·13 | 4·64 | 5·08 |
| 11 | 52 | 3·08 | 46 | 3·42 | 52 | 4·65 | 29 | 4·08 | 4·25 | 4·62 | 5·61 | 4·83 |
| 12 | 26 | 5·47 | 23 | 4·30 | 41 | 5·28 | 39 | 4·42 | 5·99 | 5·28 | 5·90 | 4·77 |
| 13 | 15 | 6·26 | 22 | 4·61 | 41 | 4·59 | 29 | 2·90 | 6·05 | 5·25 | 4·27 | 2·80 |
| 14 | 28 | 6·25 | 20 | 4·89 | 23 | 3·26 | 26 | 2·44 | 5·20 | 5·40 | 2·39 | 1·38 |
| 15 | 23 | 4·90 | 28 | 4·77 | 21 | 3·16 | 22 | 1·36 | 3·52 | 4·87 | 1·28 | 1·30 |
| 16 | 18 | 2·76 | 26 | 3·19 | 20 | 5·31 | 10 | 0·00 | 2·19 | 3·05 | 0·68 | 0·06 |
| 17 | 16 | 2·67 | 7 | (3·07) | — | — | — | — | 0·90 | 2·66 | — | — |

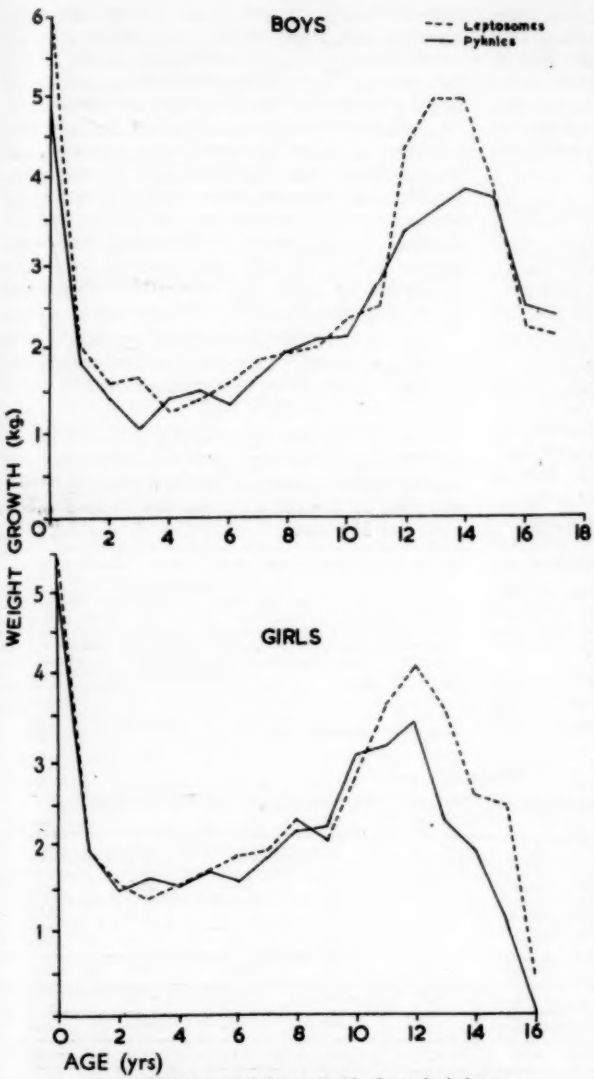


FIG. 3.—Weight growth in boys and girls of two physical types.

and in Fig. 3. The two physical types show little difference in the rate of growth from age 5 to 11+ (boys) and from age 5 to 10+ (girls), but from then onwards the leptosomes of both sexes show a somewhat greater spurt. This may be due to the fact that some children tend to increase their height without increasing comparably in weight before puberty (thus showing the leptosome habitus), and then proceed to "fill out" and gain more in weight. This is confirmed by the height increases, which are greater for the leptosomes between age 8 and age 13.

### STAGE OF DEVELOPMENT AND GROWTH

At puberty, mature children are considerably bigger than immature children of the same age (Ellis, 1946; Berry and Cowin, 1954; Scott, 1955 (boys); Wilson and Sutherland, 1950 (girls). Early maturers are also bigger from an early age (Ellis). Hammond (1955) has shown that the greater weight of children of higher social groups could be accounted for if we assumed that they matured earlier, and if we attributed to them the growth rates appropriate to their stage of development rather than to their chronological age. The cumulative effect of the greater growth due to accelerated maturity was seen to be sufficient to account for the group differences in attained weight. A similar analysis of yearly growth during the period of puberty in terms of the numbers of children at the different maturity levels and their appropriate growth has been made as follows:

The peak velocity of growth, based on children whose puberty stage is known and also on the data of Tanner (1956) may be estimated at about 7 kg. per year, and the peak occurs at 14 years (s.d. 1 year). The whole spurt lasts for about 3 years, and we can accept peak growth for the years adjacent to the peak point as 7 kg. per year, and for the outer years over which effects of the spurt are felt as 4·5 kg., giving a growth pattern of 4·5, 7, 7, 4·5 kg.

The numbers of children whose peak occurs within given ages (calculated by probit analysis assuming a normal distribution) will then be as follows:

| Age .. .. .. | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|
| Percentage .. .. | 5 | 25 | 40 | 15 | 5 |

In a 14-year-old group, therefore, 40 per cent. are at their stage of maximum spurt, 25 per cent. have had their peak growth 1 year earlier, and 5 per cent. have had it 2 years earlier, whilst 25 per cent. are at a stage 1 year before their period of maximum growth,

and 5 per cent. are 2 years before it. Similarly, in a 15-year-old group, 25 per cent. are at the peak of growth, 40 per cent. are 1 year past it, and so on. If we apply the assumed pattern of the spurt as above, with 2·7 kg. per year as the pre-pubertal and 2·2 kg. as the post-pubertal level of growth, we obtain the following expected figures for the average growth for boys:

| Age (yrs) | Weight Gain (kg.) | |
|---|---|---|
| | Calculated | Actual |
| 10+ | 2·8 | 3·0 |
| 11+ | 3·4 | 3·5 |
| 12+ | 4·7 | 4·6 |
| 13+ | 5·9 | 5·4 |
| 14+ | 5·9 | 5·8 |
| 15+ | 4·5 | 4·6 |
| 16+ | 3·1 | 3·1 |

The calculated figures agree fairly closely with the actual weight gains, the highest gains (for ages 13 and 14) being somewhat above those in Table I.

### Attained Measurements and Weight Gain

The attained measurements will determine the level of growth to be expected, because certain conditions necessarily affect both, and because growth is to some degree proportional to the size of existing structures.

Correlations between attained measurements and one-year weight gains within social classes (Table VII) are positive at the earlier years and become negative around puberty.* At younger ages larger children gain more weight than smaller children simply because this is a continuation of the process that has made them larger. Just before puberty the larger children also have their growth spurts earlier. Over the next years, the growth of children who have had their spurt and are therefore bigger is reduced, whereas those who are small through not having reached their spurt grow more when they do begin it. Similarly, in late adolescence, the smaller children continue growth longer in order to reach their mature condition—for early puberty and early attainment of adult size both occur in favoured groups in whom the early development is greater.

These correlations are of little practical use in predicting growth. Even the multiple correlations between combinations of measurements and weight gain reach only 0·40.

When growth over a period of 2 years is correlated with the original measurements (Table VIII, opposite), slightly higher figures are obtained, reaching 0·54 in the case of Weight and Hip Girth in the boys aged 8 to 11 years.

* The correlations are calculated from the groups' own means and standard deviations, and this involves a separation of the bigger attained measurements and larger weight gains in the case of the better social groups and the converse in the other groups. That is, the between-group variance and correlation have been excluded. This reduction in range will certainly give lower correlations than if they were treated as one group. (It does not, however, follow that the actual prediction of growth would be less close, since the regressions would give an expected deviation and range of growth from the mean growth for the appropriate social class rather than from a general mean, and the separate means will necessarily apply more closely.)

TABLE VII

CORRELATIONS BETWEEN BODY MEASUREMENTS AND ONE-YEAR WEIGHT GAIN DURING DIFFERENT GROWTH PHASES BY SEX

| Phase | Childhood | | Pre-adolescence | | Adolescent Spurt | | Late Adolescence | |
|---|---|---|---|---|---|---|---|---|
| Sex | Boys | Girls | Boys | Girls | Boys | Girls | Boys | Girls |
| Age Range (yrs) | 5–8+ | 5–8+ | 9–12+ | 9–11 | 13–15+ | 12–13 | 16–17 | 14–16 |
| No. of Children | 213 | 267 | 264 | 272 | 146 | 147 | 68 | 147 |
| Weight | ·24 | ·14 | ·29 | ·28 | −·20 | −·09 | −·43 | −·15 |
| Height | ·25 | ·18 | ·24 | ·23 | −·01 | ·11 | −·23 | ·04 |
| Foot Length | ·27 | ·20 | ·28 | ·19 | ·09 | ·20 | −·04 | ·11 |
| Hand Length | ·34 | ·16 | ·34 | ·21 | ·03 | ·13 | −·22 | −·03 |
| Chest Girth | ·21 | ·10 | ·24 | ·22 | −·13 | −·08 | −·06 | −·12 |
| Waist Girth | ·16 | ·10 | ·20 | ·12 | −·08 | −·20 | −·36 | −·04 |
| Hip Girth | ·24 | ·15 | ·32 | ·26 | −·09 | −·12 | −·40 | −·18 |
| Upper Arm Girth | ·34 | ·07 | ·22 | ·26 | −·19 | −·06 | −·28 | −·11 |
| Knee Girth | ·31 | ·12 | ·23 | ·28 | −·11 | −·12 | −·03 | −·05 |
| Intertrochanteric Breadth | ·31 | ·21 | ·31 | ·28 | −·16 | −·08 | −·33 | −·12 |
| Interacromial Breadth | ·21 | ·22 | ·36 | ·19 | −·04 | −·05 | −·10 | −·05 |

TABLE VIII

CORRELATIONS BETWEEN CERTAIN BODY MEASUREMENTS, AND WEIGHT GAIN OVER 2 YEARS, BY SOCIAL GROUP AND SEX

| Measurement | Social Group | Age (yrs) 5–7+ Boys | 5–7+ Girls | 8–11+ Boys | 8–11+ Girls | 12–15+ Boys | 12–15+ Girls |
|---|---|---|---|---|---|---|---|
| Weight .. | A | — | ·23 | ·40 | ·15 | −·37 | ·25 |
| | B | ·44 | ·40 | ·54 | ·40 | — | — |
| Height .. | A | — | ·19 | ·32 | ·29 | −·14 | ·37 |
| | B | ·37 | ·44 | ·47 | ·24 | — | — |
| Foot Length | A | — | ·06 | ·34 | ·33 | ·04 | ·37 |
| | B | ·27 | ·34 | ·38 | ·27 | — | — |
| Hip Girth .. | A | — | ·26 | ·31 | ·15 | −·26 | ·30 |
| | B | ·34 | ·43 | ·46 | ·40 | — | — |
| Knee Girth .. | A | — | ·18 | ·37 | ·15 | −·12 | ·31 |
| | B | ·38 | ·27 | ·46 | ·50 | — | — |
| Inter-trochanteric Breadth .. | A | — | ·25 | ·35 | ·15 | −·25 | ·31 |
| | B | ·36 | ·46 | ·54 | ·33 | — | — |
| Interacromial Breadth .. | A | — | ·20 | ·33 | ·16 | −·17 | ·36 |
| | B | ·35 | ·35 | ·40 | ·25 | — | — |
| No. of Children .. | A | — | 36 | 121 | 144 | 134 | 129 |
| | B | 98 | 104 | 112 | 141 | — | — |

*Note:* Correlations are within year figures combined over the age groups shown; *e.g.* age group 12–15+ indicates growth from ages 12–14, 13–15, 14–16, and 15–17 years.

These correlations are still of limited use in reducing the range of expected variation in growth, and the highest multiple correlations are only a little over 0·6.

There is little difference in predictability of growth for boys and girls, and also little difference from age 5 until the pubertal spurt begins. Throughout the age range, Social Group B (the poorer group) has higher correlations than the Social Group A, possibly because in this group some children are very small, on account of a depressed rate of growth in the past, and their low rate continues.

## GROWTH CONSISTENCY

### *An Interpretation of the Variability of Growth over Short and Long Periods*

The consistency in growth over different intervals can be determined by correlating the growth increases from one period to another; but where this may not be possible, as, for example, when the same children are not measured over the whole period, it can be inferred from the relations between growth variability during short and long periods.

The standard deviations of growth over 2 years or longer will equal the sum of those of successive yearly increases if the correlation between the separate years' growth is perfect. With zero correlation the *variance* will be additive and therefore the standard deviations will be equal to the square root of the sum of the variances. Negative correlation will result in a reduction of the overall variance compared with either of the yearly values.*

In the group of infants measured annually (Hammond, 1955), it was found that the sums of the variances of the yearly growth equalled the variances of the corresponding periods from birth to 5 years, indicating almost zero correlation between growth in any year compared with the next. Similarly the variances of the separate year's growth calculated from Table I are less than the variances of the 3-year growth up to age 12 and slightly greater from age 13 to age 15. These results show that growth from year to year has a low positive correlation up to age 12. After this, until age 15, negative correlations occur, since children tend to grow rapidly in one year and less rapidly in another, reflecting the growth trough before the pubertal spurt or different stages of the spurt.

The correlations between annual weight and height gain in non-adjacent periods for the data of Low (1952) and Hammond (1953) were as follows:

| Gain | Sex | No. of Children | Birth 1 yr with 2–3 yrs r | 1–2 yrs with 3–4 yrs r | 2–3 yrs with 4–5 yrs r | 8–9 yrs with 10–11 yrs r |
|---|---|---|---|---|---|---|
| Weight | Boys | (66) | −0·29 | −0·53 | −0·04 | (100) 0·118 |
| | Girls | (60) | −0·33 | −0·09 | −0·14 | (67) 0·355 |
| Height | Boys | (66) | −0·18 | +0·01 | −0·16 | — |
| | Girls | (60) | 0·10 | 0·04 | 0·06 | — |

The author's own data gave correlations between growth from birth to 2 years and growth from 3 to 5 years, ranging from 0·08 to 0·26 for a number of different physical measurements.

The correlations are so low as to suggest that growth over different periods, even within the same stages of growth, is affected by conditions which vary from one moment to the next. Other body measurements show much the same unpredictability.

The correlations between growth from birth to 1 year and birth to 5 years were:

Weight: boys 0·47
girls 0·59
Height: boys 0·63
girls 0·66

* The relation is as follows:
Variance of Combined Growth = $Vs_1 + Vs_2 + 2r\sqrt{Vs_1\ Vs_2}$, where $Vs_1$ and $Vs_2$ are variances of separate annual growth increases, and $r$ is the correlation between them.

## Discussion

Growth velocity—to use Tanner's term—has in the past been treated less adequately than attained size. This, of course, is because studies of growth require at least two measurements and a time interval and are therefore more difficult to carry out.

After the fourth year of life the variability of annual weight increase is so high that any measureable increase, however small, lies within the "statistically normal" range ($\pm 2$ s.d.). Annual increase in height is much less variable and failure to gain in any year is rare (as rare as failure to gain weight over 3 years). The effect of age on growth rates is much less than its effect on attained size (which represents the cumulative result of growth from conception). The fairly constant level of growth over the period from age 5 to age 8 or 9 permits the comparison of groups of children within this range, even when age means or distributions are not exactly the same. The growth pattern for the years preceding puberty is not distinct enough to enable us to estimate from it the maturity level of the individual, or to say when his spurt is likely to occur. There is, however, some evidence of a slight trough in growth just before the pubertal spurt begins.

The variance of growth can be used to indicate whether differences in measurements between individuals or groups could have arisen within a particular period. If limiting conditions of *growth* over any period (*e.g.* mean $\pm 2$ s.d.) are applied to the differences between the attained measurements, it is possible to say whether the difference between individuals or groups could be accounted for by growth during the period tested. And the extent to which these ranges overlap will indicate the likelihood that the difference has arisen during the given period. Conversely, it is possible to show how great the growth must have been during any period for present differences to have arisen within that period.

It would be expected that the whole course of past growth from birth would give a very strong indication of the growth during subsequent years, yet correlations between attained measurements and later growth are surprisingly low. Tanner, Healy, Lockhart, MacKenzie, and Whitehouse (1956) found that the prediction of adults' measurements from measurements made during infancy was little improved by taking into account the course of growth from birth. The correlations obtained could be attributed in large part to the inclusion of the earlier measurements in the later ones (nearly half the total growth in stature from birth having already occurred by age 5). Growth from birth to 5 years can only be predicted from the first year's growth to the extent of its contribution to the common variance, while growth during the first 5 years has a negligible predictive value for subsequent growth. This is confirmed by the fact that correlations between the gains in adjacent years or within a narrow age range are less than the correlations between the first year's growth and the growth from birth to 5 years (where overlap occurs).

Growth during one year is, of course, only one possible interval which might be considered. Just as it reflects conditions acting over a shorter time than attained size, so growth during still shorter intervals will further localize conditions. So far, the main use for these shorter intervals has been in studying growth in the first year of life and seasonal fluctuations. Half-yearly or even quarterly growth can also be useful in the adolescent period.

## Summary

The means and standard deviations of weight and height growth are given for periods of 1, 2, and 3 years from birth to 18 years. The yearly growth is also differentiated in terms of two social groups, two physical types, and different nutritional classes.

Growth is greatest during the first year both in absolute amounts and relative to its variability. At adolescence, when growth is almost as great, its variability is much higher, largely because of the different time of onset of the spurt. For this reason different standards should be used for pre- and post-pubescent children apart from age.

Children in higher social groups and those of better nutritional status grow more, as we should expect, but in the former case the excess growth is mainly in height, and in the latter it is mainly in weight. Leptosome and pachysome types (eurysomes or pyknics) differ little in weight growth up to age 12, but after this age children whose height growth has tended to precede weight growth and who are therefore more leptosome tend to gain more weight.

The growth over 2- and 3-year intervals is such as to suggest that growth in each individual year is uncorrelated.

Correlations between attained measurements and weight gain (within the same social class) are very low, rarely exceeding 0·4 for 1 year's growth and 0·5 for 2 years' growth. At puberty they become negative.

Correlations between growth at one period and another are mostly around zero and they are again negative at puberty.

Differences in weight gain between groups at pubertal ages can be estimated from the numbers at

the different stages of puberty, assuming a definite spurt pattern.

By relating differences in measurements to the variability of growth it is possible to separate influences of short or long duration.

I wish to thank Dr. E. R. Bransby of the Ministry of Health who initiated these studies, the National Physical Laboratory for machine analysis of much of the data, and Mr. T. O'Hara, Ministry of Health, for his helpful suggestions at the later stages.

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# EXAMINATION OF THE ASSOCIATION BETWEEN HOUSING CONDITIONS AND PULMONARY TUBERCULOSIS IN GLASGOW

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It has been generally accepted that there is some association between unsatisfactory housing conditions and pulmonary tuberculosis. Lack of sunlight and deficient ventilation, often aggravated by overcrowding, may lower resistance, and overcrowding in the presence of an infectious case increases the risk of massive infection. High population density also favours the spread of infection. Yet the exact role played by poor housing in the incidence of pulmonary tuberculosis has been a matter of much speculation.

McKinlay (1947) drew attention to a "dissimilarity" in the trends of mortality from tuberculosis and of housing as measured by the average number of persons per room and the proportion of the population overcrowded over the 20-year period 1911 to 1931. He concluded that:

"... If adverse housing is in any way approaching the importance generally believed in determining the level of mortality from this disease, other factors must be operative—factors, moreover, which must be negatively correlated with the housing status (*i.e.*, worst where housing is best) and of sufficient importance completely to obliterate in these data any evidence of a housing influence good or bad".

Stein (1950) studied the influence of socio-economic conditions in Glasgow on the ward tuberculosis rates from 1930 to 1947 and concluded that:

"In the wards of Glasgow, the investigation of small, homogeneous areas reveals that the inequalities of incidence in this disease are very largely accounted for by disparities in social conditions. ... The relationship of respiratory tuberculosis with the social complex demonstrates the important role played in Glasgow by housing conditions. Ordinary density of dwelling occupation, [average number of persons per house], together with overcrowding, represents the dominant influence in infection and in death from this disease".

On the other hand, however, Brett and Benjamin (1957), in a study of the association of housing conditions with the prevalence of tuberculosis in the Metropolitan Borough of Islington, found "no gradient in tuberculosis morbidity in relation to rising housing density".

In the present paper, notifications of pulmonary tuberculosis in Glasgow during 1951 and 1952 are examined in relation to housing conditions in the 37 wards of the city. A more detailed examination is made of notifications during 1951 in two districts of the city (each comprising two adjacent wards), one with an exceptionally high and the other with a low incidence of the disease.

## Ward Case-Rates related to Housing Conditions

Table I (opposite) gives the ward populations as at the 1951 Census (General Registry Office, Edinburgh, 1952), the ward case-rates for pulmonary tuberculosis per 10,000 of the population, adjusted for age and sex, for the combined years 1951 and 1952, the difference between the adjusted ward rates and the city rate expressed in terms of the standard errors, the average number of rooms per house, the average number of persons per room, and the percentage of the 1951 population in private households living more than two persons per room. Adjusting factors for age and sex were calculated on the age and sex distributions of the ward populations at the 1951 Census, The adjusted ward case-rates for pulmonary tuberculosis per 10,000 of the population range from 10·8 to 28·5. Six wards have case-rates less than the city rate and three wards case-rates greater than the city rate by as much as twice the standard error.

The number of rooms per house has a high negative correlation and the number of persons per

TABLE I

WARD CASE-RATES RELATED TO HOUSING CONDITIONS ADJUSTED FOR AGE AND SEX (GLASGOW 1951 AND 1952)

| City Wards | | Case-Rate per 10,000 Population | Difference of Adjusted Ward Case-Rates from City Rate in Terms of Standard Errors $x$ | Rooms per House $y_1$ | Persons per Room $y_2$ | Percentage of Population in Private Households (1951 Census) living More than Two Persons per Room $y_3$ |
|---|---|---|---|---|---|---|
| Number | Population | | | | | |
| 1 | 42,609 | 22·5 | +0·91 | 2·63 | 1·47 | 27·3 |
| 2 | 21,578 | 18·1 | −0·80 | 2·66 | 1·37 | 24·0 |
| 3 | 40,621 | 19·2 | −0·61 | 1·90 | 1·80 | 43·2 |
| 4 | 26,273 | 24·7 | +1·48 | 2·24 | 1·58 | 37·2 |
| 5 | 40,171 | 21·9 | +0·59 | 2·05 | 1·73 | 40·8 |
| 6 | 26,944 | 18·5 | −0·73 | 2·87 | 1·16 | 16·2 |
| 7 | 24,235 | 24·9 | +1·53 | 3·32 | 1·22 | 17·3 |
| 8 | 27,998 | 18·9 | −0·60 | 2·11 | 1·59 | 32·2 |
| 9 | 35,649 | 19·4 | −0·50 | 3·01 | 1·40 | 18·6 |
| 10 | 35,005 | 27·3 | +2·78 | 2·28 | 1·51 | 32·3 |
| 11 | 20,089 | 20·7 | +0·03 | 2·67 | 1·35 | 29·4 |
| 12 | 31,902 | 21·4 | +0·33 | 2·41 | 1·50 | 33·2 |
| 13 | 23,758 | 22·2 | +0·56 | 3·94 | 0·89 | 8·6 |
| 14 | 27,229 | 28·5 | +2·91 | 2·08 | 1·72 | 41·6 |
| 15 | 26,946 | 23·0 | +0·87 | 2·25 | 1·51 | 36·4 |
| 16 | 45,929 | 23·6 | +1·51 | 2·89 | 1·46 | 24·2 |
| 17 | 28,817 | 15·0 | −1·91 | 2·52 | 1·26 | 26·8 |
| 18 | 25,515 | 16·7 | −1·38 | 2·52 | 1·42 | 28·0 |
| 19 | 21,032 | 12·2 | −2·48 | 4·16 | 0·68 | 2·0 |
| 20 | 23,376 | 15·7 | −1·58 | 3·74 | 0·85 | 8·4 |
| 21 | 26,814 | 18·7 | −0·65 | 2·45 | 1·29 | 29·6 |
| 22 | 23,241 | 17·8 | −0·91 | 3·12 | 1·09 | 18·5 |
| 23 | 30,198 | 14·2 | −2·49 | 3·34 | 1·15 | 10·1 |
| 24 | 17,530 | 16·6 | −1·18 | 3·45 | 1·16 | 10·4 |
| 25 | 30,965 | 20·7 | +0·07 | 1·81 | 1·82 | 44·2 |
| 26 | 36,648 | 25·5 | +2·13 | 2·36 | 1·66 | 41·9 |
| 27 | 26,895 | 21·4 | +0·31 | 2·34 | 1·56 | 35·1 |
| 28 | 28,124 | 17·6 | −1·09 | 2·43 | 1·41 | 30·5 |
| 29 | 35,152 | 21·1 | +0·25 | 2·37 | 1·62 | 38·6 |
| 30 | 25,132 | 20·2 | −0·14 | 2·55 | 1·38 | 22·3 |
| 31 | 40,448 | 15·6 | −2·21 | 3·88 | 0·98 | 5·2 |
| 32 | 39,956 | 16·0 | −2·01 | 4·41 | 0·98 | 5·7 |
| 33 | 22,529 | 12·7 | −2·42 | 3·44 | 0·84 | 3·5 |
| 34 | 39,717 | 22·5 | +0·90 | 3·43 | 1·30 | 18·5 |
| 35 | 26,377 | 16·5 | −1·40 | 2·56 | 1·22 | 15·6 |
| 36 | 25,578 | 15·1 | −1·85 | 3·90 | 0·80 | 1·4 |
| 37 | 21,787 | 10·8 | −3·02 | 4·01 | 0·78 | 3·8 |
| City | 1,089,767 | 20·5 | — | 2·82 | 1·27 | 24·4 |

room and the percentage of the population living more than two per room (overcrowding) have high positive correlations with the ward incidence of pulmonary tuberculosis, expressed as the difference between the adjusted ward case-rates and the city rate in terms of the standard errors (Table II; Figs 1, 2, and 3, overleaf).

The positive correlation with persons per room and with overcrowding is greater than the negative correlation with the average number of rooms per house. The association between these overcrowding indices and ward case-rates appears to be restricted to the 21 wards of the city with case-rates less than the city rate: in the sixteen wards with case-rates greater than the city rate there is no significant correlation.

To examine in more detail the influence of housing conditions, two districts were selected for special study. One, District A, comprised the adjoining Wards 10 and 14 where the incidence of pulmonary tuberculosis was high, and the other, District B, the adjoining Wards 17 and 18 where the incidence was low. In 1951 the case-rate for pulmonary tuberculosis for the city was 20·3 per 10,000 of the

TABLE II

CORRELATION COEFFICIENTS CALCULATED FROM DATA IN TABLE I

*Correlation Coefficients for the* 37 *Wards of the City*

| | |
|---|---|
| $r_{xy_1} = -0·5519$ | $r_{y_1y_2} = -0·9169$ |
| $r_{xy_2} = 0·6735$ | $r_{y_1y_3} = -0·9351$ |
| $r_{xy_3} = 0·6687$ | $r_{y_2y_3} = 0·9565$ |

*Correlation Coefficients for the* 21 *Wards of the City having Case-Rates Less than the City Rate*

| | |
|---|---|
| $r_{x'y'_1} = -0·7220$ | $r_{y'_1y'_2} = -0·8973$ |
| $r_{x'y'_2} = 0·7553$ | $r_{y'_1y'_3} = -0·9303$ |
| $r_{x'y'_3} = 0·7167$ | $r_{y'_2y'_3} = 0·9333$ |

*Correlation Coefficients for the* 16 *Wards of the City having Case-Rates Greater than the City Rate*

| | |
|---|---|
| $r_{x''y''_1} = -0·0898$ | $r_{y''_1y''_2} = -0·9443$ |
| $r_{x''y''_2} = 0·1317$ | $r_{y''_1y''_3} = -0·9670$ |
| $r_{x''y''_3} = 0·0890$ | $r_{y''_2y''_3} = 0·9530$ |

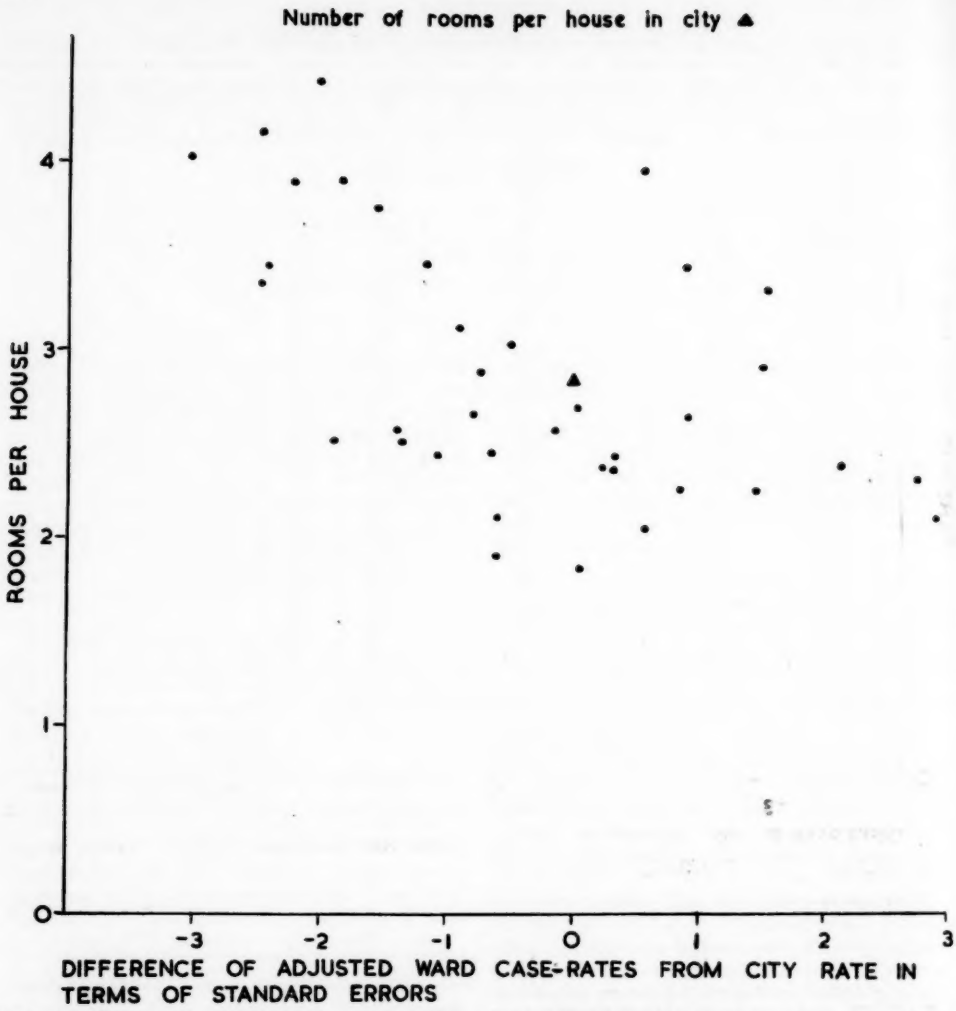


FIG. 1.—Adjusted ward case-rates for pulmonary tuberculosis (Glasgow, 1951 and 1952) expressed as the difference of the ward rates from the city rate in terms of the standard errors and the number of rooms per house.

population: in districts A and B it was 26·1 and 17·6 respectively. It must be remembered that at the Census in 1951, 47·3 per cent. of houses in the city were of one and two rooms, so that, in addition to social and economic circumstances, availability of accommodation in Glasgow plays a large part in determining the size of house a family occupies (Table III, opposite).

When 1951 notifications in District A came to be individually reviewed, two errors were found in location of cases at the periphery of the district, and one case of tuberculous disease of the hip joint had been wrongly classified as respiratory disease. After these errors had been corrected, and two cases living in common lodging-houses had been excluded, there remained for analysis 156 notified cases in

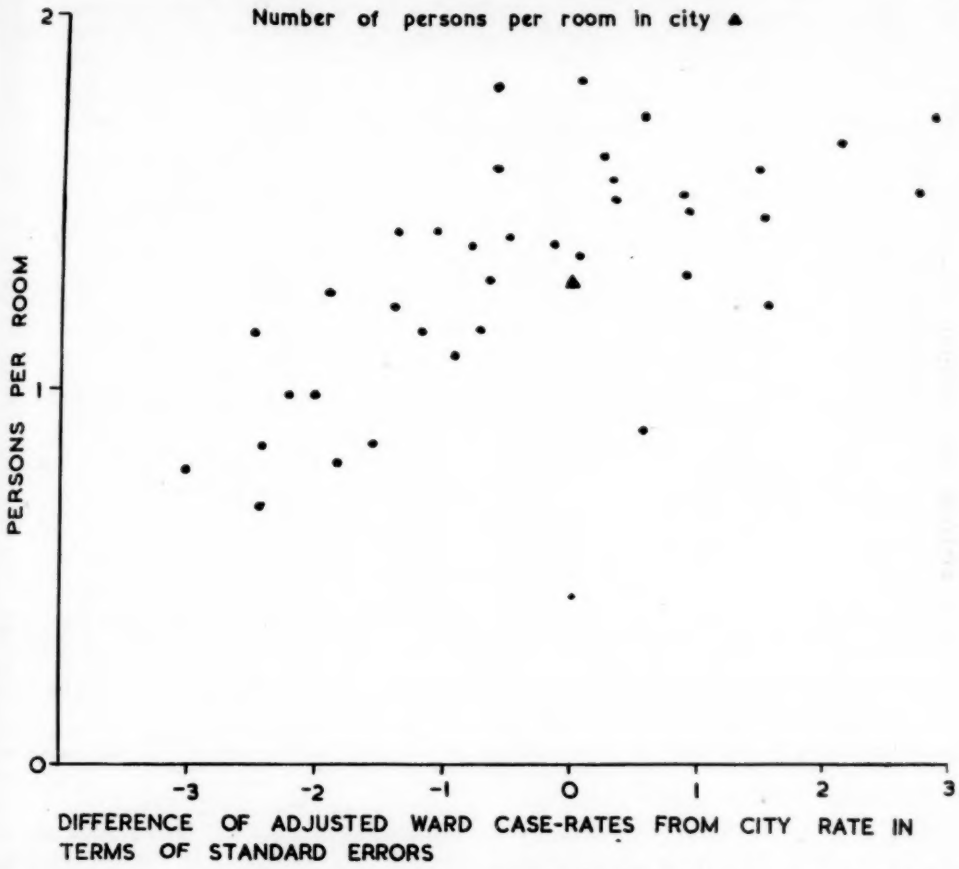


FIG. 2.—Adjusted ward case-rates for pulmonary tuberculosis (Glasgow, 1951 and 1952) expressed as the difference of the ward rates from the city rate in terms of the standard errors and the number of persons per room.

TABLE III

NUMBER OF ROOMS PER HOUSE IN DISTRICTS A AND B AND IN GLASGOW AS A WHOLE

| Area | Case-Rates per 10,000 1951 | Percentage of Occupied Houses (1951 Census) with: | | | | | No. of Houses in Area |
|---|---|---|---|---|---|---|---|
| | | One Room | Two Rooms | Three Rooms | Four Rooms and Over | All Houses | |
| Glasgow .. .. | 20·3 | 11·0 | 36·3 | 28·2 | 24·5 | 100·0 | 294,467 |
| District A .. .. | 26·1 | 16·7 | 55·6 | 21·9 | 5·8 | 100·0 | 17,044 |
| District B .. .. | 17·6 | 11·8 | 49·1 | 26·3 | 12·7 | 100·0 | 14,915 |

District A and 88 notified cases in District B. In the analysis which follows the terms "tuberculous cases", "tuberculous houses", and "tuberculous households" refer to these notified cases and to the houses and households in which they lived. It has not been possible to allow for age and sex.

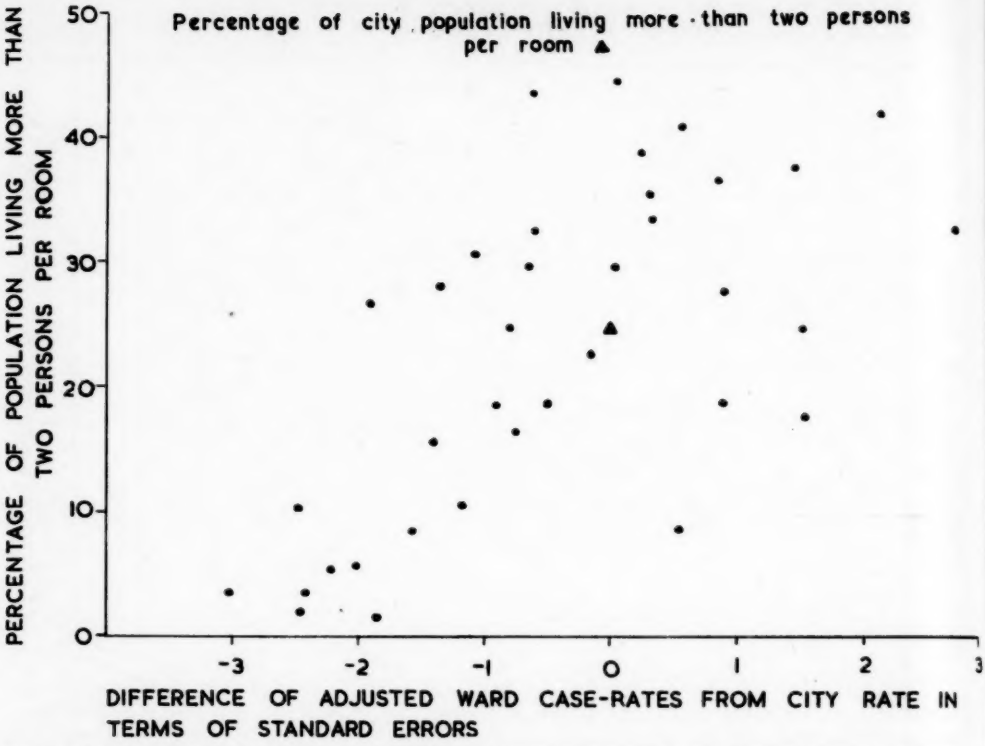


FIG. 3.—Adjusted ward case-rates for pulmonary tuberculosis (Glasgow, 1951 and 1952) expressed as the difference of the ward rates from the city rate in terms of the standard errors and the percentage of the population living more than two persons per room.

NUMBER OF ROOMS IN TUBERCULOUS HOUSES AND NUMBER OF ROOMS OCCUPIED BY HOUSEHOLDS OF TUBERCULOUS CASES

The number of houses of one, two, three, and four or more rooms, and of households occupying one, two, three, and four or more rooms, with the number of persons occupying corresponding accommodation are given in Table IV (opposite) with the notifications of pulmonary tuberculosis in 1951 and the case-rates per 10,000 of the population. The case-rates in houses of one room and of four or more rooms and in households occupying one room and four or more rooms in District A may appear somewhat high, but the numbers are small and the differences not significant.

Tables V and VI (opposite) give the observed and expected numbers of notifications according to rooms per house and rooms per household; the expected number is based on the proportion of the district populations (Census, 1951) living in corresponding accommodation. In the two districts, though the numbers are small, there is no evidence that either the number of rooms in the tuberculous house or the number of rooms occupied by the tuberculous household has influenced the incidence of the disease.

SIZE OF FAMILY AND OVERCROWDING.—Irrespective of the number of rooms occupied, the average number of persons in tuberculous households was, in both districts, consistently greater than that in private households generally (Table VII, opposite).

In 1951, 14·9 per cent. of the population in Glasgow were in the age group 15–24 years, but this age group accounted for 34 per cent. of the notifications of pulmonary tuberculosis (Table VIII, opposite). Only 16 per cent. of the persons in this age group were married, compared with 69 per cent. of

TABLE IV

PRIVATE HOUSES, PERSONS IN PRIVATE HOUSES, PRIVATE HOUSEHOLDS, AND PERSONS IN PRIVATE HOUSEHOLDS (1951 CENSUS) RELATED TO NOTIFICATIONS

| District | | A | | | | B | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | No. of Private Houses | No. of Persons | No. of Tuberculous Cases | Case-Rate per 10,000 | No. of Private Houses | No. of Persons | No. of Tuberculous Cases | Case-Rate per 10,000 |
| No. of Rooms in House | 1 | 2,839 | 7,568 | 24 | 31·7 | 1,766 | 4,617 | 6 | 13·0 |
| | 2 | 9,482 | 32,204 | 74 | 23·0 | 7,323 | 23,303 | 45 | 19·3 |
| | 3 | 3,732 | 14,830 | 39 | 26·3 | 3,930 | 14,443 | 25 | 17·3 |
| | 4 and Over | 991 | 5,088 | 19 | 37·3 | 1,896 | 7,701 | 12 | 15·6 |
| Total Houses .. .. .. | | 17,044 | 59,690 | 156 | 26·1 | 14,915 | 50,064 | 88 | 17·6 |
| No. of Rooms occupied by Household | 1 | 3,648 | 9,555 | 33 | 34·5 | 2,274 | 5,752 | 11 | 19·1 |
| | 2 | 9,556 | 32,139 | 73 | 22·7 | 7,427 | 23,441 | 45 | 19·2 |
| | 3 | 3,630 | 14,070 | 35 | 24·9 | 3,873 | 13,956 | 21 | 15·0 |
| | 4 and Over | 856 | 3,926 | 15 | 38·2 | 1,823 | 6,915 | 11 | 15·9 |
| Total Households .. .. | | 17,690 | 59,690 | 156 | 26·1 | 15,397 | 50,064 | 88 | 17·6 |

TABLE V

NOTIFICATIONS ACCORDING TO ROOMS PER HOUSE

| District | | A | | B | |
|---|---|---|---|---|---|
| | | Notifications | | Notifications | |
| | | Observed | Expected* | Observed | Expected* |
| No. of Rooms per House | 1 | 24 | 19·8 | 6 | 8·1 |
| | 2 | 74 | 84·2 | 45 | 41·0 |
| | 3 | 39 | 38·8 | 25 | 25·4 |
| | 4 and Over | 19 | 13·3 | 12 | 13·5 |
| Total Private Houses | | 156 | 156·0 | 88 | 88·0 |

* The expected number is based on the House Population (Census).
*District A:* $\chi^2_5 = 4{\cdot}57$; $0{\cdot}2 < P < 0{\cdot}3$
*District B:* $\chi^2_5 = 1{\cdot}11$; $0{\cdot}7 < P < 0{\cdot}8$

TABLE VI

NOTIFICATIONS ACCORDING TO ROOMS PER HOUSEHOLD

| District | | A | | B | |
|---|---|---|---|---|---|
| | | Notifications | | Notifications | |
| | | Observed | Expected* | Observed | Expected* |
| No. of Rooms Occupied by Household | 1 | 33 | 25·0 | 11 | 10·1 |
| | 2 | 73 | 84·0 | 45 | 41·2 |
| | 3 | 35 | 36·8 | 21 | 24·5 |
| | 4 and Over | 15 | 10·3 | 11 | 12·2 |
| Total Private Households .. | | 156 | 156·0 | 88 | 88·0 |

* The expected number is based on the Household Population (Census)
*District A:* $\chi^2_5 = 6{\cdot}23$; $0{\cdot}1 < P < 0{\cdot}2$
*District B:* $\chi^2_5 = 1{\cdot}05$; $0{\cdot}7 < P < 0{\cdot}8$

TABLE VII

AVERAGE NUMBER OF PERSONS PER HOUSEHOLD

| District | | A | | B | |
|---|---|---|---|---|---|
| | | All Private Households | Tuberculous Households | All Private Households | Tuberculous Households |
| No. of Rooms Occupied by Household | 1 | 2·6 | 3·3 | 2·5 | 2·8 |
| | 2 | 3·4 | 4·0 | 3·2 | 4·2 |
| | 3 | 3·9 | 4·8 | 3·6 | 5·7 |
| | 4 and Over | 4·6 | 5·8 | 3·8 | 5·6 |
| All Households .. | | 3·4 | 4·2 | 3·3 | 4·5 |

those in the following decade. Families with adolescent and young adult members, of whom only a small proportion are married, are usually approaching their maximum size, and since the incidence of disease in the adolescent and young adult age group is high, it would appear to follow that the average size of families in which a case of pulmonary tuberculosis had occurred would necessarily be larger than the average size of other families in the area.

Where the number of rooms per house in an area is small, it is to be expected, if the average tuberculous household is larger than the average household, that tuberculous households will show more overcrowding. A comparison of the proportion of tuberculous cases overcrowded with the proportion of the

TABLE VIII

PERCENTAGE OF POPULATION AND OF NOTIFICATIONS OF PULMONARY TUBERCULOSIS BY AGE GROUP AND SEX, GLASGOW, 1951

| Sex | | Male | | Female | | Both | | Per cent. of Population Married |
|---|---|---|---|---|---|---|---|---|
| | | Population | Notifications | Population | Notifications | Population | Notifications | |
| Age Group (yrs) | Under 15 .. | 26·4 | 10·9 | 23·4 | 14·7 | 24·8 | 12·7 | — |
| | 15–24 .. | 14·5 | 26·3 | 15·2 | 42·7 | 14·9 | 34·0 | 16·0 |
| | 25–34 .. | 14·8 | 16·2 | 14·4 | 22·9 | 14·6 | 19·4 | 69·0 |
| | 35 and Over | 44·3 | 46·6 | 47·0 | 19·7 | 45·7 | 33·9 | 67·9 |
| | All Ages .. | 100·0 | 100·0 | 100·0 | 100·0 | 100·0 | 100·0 | 43·5 |

population overcrowded may be expected to yield evidence of the association of tuberculosis with overcrowding, but, on the basis of the previous argument, the overcrowded population in an area would be likely to contain a larger proportion of adolescents and young adults. Therefore, to get a true estimate of the importance of overcrowding as a factor, an adjustment for the age and sex of the population overcrowded and of the population not overcrowded would be required. The data for such an adjustment were not available in the present analysis.

Overcrowding.—In District A, 36·8 per cent. of the total population but only 29·5 per cent. of the tuberculous cases were overcrowded (*i.e.* living more than two persons per room). Of all private households in the district, 23·4 per cent. were overcrowded compared with 29·5 per cent. of tuberculous households. These differences are not statistically significant. In District B, on the other hand, 27·5 per cent. of the total population and 37·5 per cent. of tuberculous cases were overcrowded, as were 17 per cent. of private households and 37·2 per cent. of tuberculous households. The difference in both these instances is significant of an association between pulmonary tuberculosis and overcrowding.

Over one-half of households in the city (Census 1951) occupied one or two rooms and of these one- and two-roomed households 44·5 and 18·9 per cent. respectively were overcrowded. As the number of rooms increases, the percentage of overcrowding falls rapidly. It is, therefore, the households living in one and two rooms that contribute largely to the state of overcrowding in the city. And if overcrowding *per se* had been the important factor, an appreciably higher proportion of households occupying one and two rooms might have been expected to be attacked. In District B 64·0 per cent. of tuberculous households and 63·0 per cent. of all households occupied no more than two rooms, and no association was found between the number of rooms occupied by the household and the occurrence of tuberculosis.

It would appear that the association with overcrowding in District B merely reflected the larger size of the tuberculous family and that the population in both districts shared in the general incidence of the disease in the district independent of overcrowding.

Contact Cases and Overcrowding.—The term "contact case" refers to a case of pulmonary tuberculosis living at the time of onset or within 5 years of onset in the same house as a case of pulmonary tuberculosis (Table IX). In 89·1 per cent. of the contact cases as thus defined, the previous case was a member of the patient's immediate family. In no instance had a contact been rehoused under the tuberculosis scheme. Since there was no appreciable difference in the proportion of contact cases occurring in the two districts, they were considered together for the purpose of this section. Where two cases were notified in a household during the year and the first case was a primary notification, the household was recorded twice, it was recorded only once where more than one contact case arose.

When overcrowding (more than two persons per room) in the households of contact cases was compared with overcrowding in those households where there had been no previous case (33·3 and 32·4 per cent. respectively), no significant association with overcrowding was found (Table X, opposite).

In 26 households, the contact was living in the same house with a case of pulmonary tuberculosis at the time of onset; in fifteen of these households (four living more than two persons per room), contact was with a sputum-positive case, and in the remaining eleven (six living more than two persons per room), contact was with a sputum-negative case.

TABLE IX

CONTACT CASES OF PULMONARY TUBERCULOSIS LIVING AT TIME OR WITHIN 5 YEARS OF ONSET IN SAME HOUSE, WITH A CASE OF PULMONARY TUBERCULOSIS

(Numbers of households affected are given in brackets)

| District | | A | | | | B | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Sputum | | All Cases | Per Cent. of Total | Sputum | | All Cases | Per Cent. of Total |
| | | Positive | Negative | | | Positive | Negative | | |
| History of Contact | At Onset | 13 (11) | 8 (8) | 21 (19) | 13·6 (12·4) | 5 (4) | 4 (3) | 9 (7) | 10·2 (8·1 |
| | Within 5 years of Onset | 12 (12) | 4 (4) | 16 (16) | 10·3 (10·5) | 6 (6) | 3 (3) | 9 (9) | 10·2 (10·5) |
| | No Contact History as Defined | — | — | 118 (118) | 76·1 (77·1) | — | — | 70 (70) | 79·6 (81·4) |
| | All Cases | 25 (23) | 12 (12) | 155*(153) | 100·0 (100·0) | 11 (10) | 7 (6) | 88 (86) | 100·0 (100·0) |

* One case excluded, a widow, who lived alone and who died in a general hospital, and of whom no information as to previous contact was available.

TABLE X

COMPARISON OF OVERCROWDING IN HOUSEHOLDS OF "CONTACT" CASES WITH HOUSEHOLDS OF CASES HAVING "NO CONTACT"

| No. of Persons Living per Room | Contact Households | | | Households with "No Contact" | All Tuberculous Households |
|---|---|---|---|---|---|
| | All Cases | Sputum + | Sputum − | | |
| More than Two | 17 | 10 | 7 | 61 | 78 |
| Not more than Two | 34 | 23 | 11 | 127 | 161 |
| All Households | 51 | 33 | 18 | 188 | 239 |
| Percentage Overcrowded | 33·3 | 30·3 | 38·9 | 32·4 | 32·6 |

These numbers do not reveal any association between overcrowding in the households of contact cases as compared with overcrowding in households where there had been no previous case.

The total number of persons in the households of contact cases of pulmonary tuberculosis was 282, of whom 172 lived not more than two persons per room. In the group of 172 persons who were not overcrowded, there were 37 contact cases (21·5 per cent.), while in the remaining group of 110 persons who were overcrowded, there were eighteen contact cases (16·4 per cent.). Again no association between the incidence of contact cases of pulmonary tuberculosis and overcrowding is present.

While no association between the occurrence of contact cases of pulmonary tuberculosis and overcrowding has been established, the problem is complicated by the rehousing of patients in an actively infectious stage who were unable to have a room to themselves, and further complicated by delays in rehousing from financial reasons and from difficulties in meeting the wishes of the patient and his family in such matters as distance from work, nearness of relatives, and congeniality of surroundings. Any conclusions as to the influence of overcrowding must be treated with reserve.

The risk to household contacts with persons suffering from pulmonary tuberculosis is very great. The 244 cases notified from the two districts in 1951, included 55 cases living or having lived within 5 years of onset in the same house with a case of pulmonary tuberculosis, and in 26 households the person or persons with whom the case or cases had been in contact was still living there. These 244 cases were associated with 767 household contacts. The 55 new contact cases occurred among 796 family contacts of known cases of pulmonary tuberculosis, which gives a case-rate of 691 per 10,000. The total population of the two districts was 109,754, and in this population 244 cases were notified, giving a case-rate of 22·2 per 10,000. Thus the estimated case-rate in family contacts is about thirty times that in the general population.

### FITNESS OF A HOUSE AS A POSSIBLE INFLUENCE ON THE INCIDENCE OF PULMONARY TUBERCULOSIS

Ward 10 of District A was surveyed in detail as to the standard of housing in 1949, and Ward 14 in 1950. Measures were taken, as far as was practicable, to keep the surveys up-to-date, and the figures quoted are for the end of 1951. Ward 18 of District B was surveyed in the latter half of 1952. Ward 17 of District B was not surveyed and has been excluded from the analysis. It was known that in Ward 17 there were only 47 unfit houses, twenty of one room, 26 of two rooms, and one of three rooms. The built-up area of Ward 18 covered only a part of the total area of the Ward. A squatters' camp, remote from the built-up area and with separate access to the City, in which no case of tuberculosis was notified in 1951, has been excluded from the survey figures, as have the houses of the married quarters of Maryhill Barracks.

There is a small discrepancy of 1 per cent. between the total number of houses in the survey and the number obtained at the Census in both wards of District A, and in Ward 18 of District B.

CLASSIFICATION OF HOUSES.—For the purpose of these surveys the houses were classified according to four standards:

*Standard.*—Houses containing all modern conveniences, including separate water-closet, bathroom, adequate food storage accommodation, adequate cooking facilities, and hot and cold water supply. Such houses seldom have less than three rooms.

*Substandard "A".*—Houses falling short in some degree of the standard house, but situated in a building of good fabric which could be adapted to provide houses of standard type. Such houses may have only one room.

*Substandard "B".*—Houses which, while not considered unfit, are unsatisfactory. They fall short of the standard type, and because of the age of the building and the condition of the fabric are not suitable for reconstruction.

*Unfit.*—Houses unfit for human habitation because of defective design or the degree of sanitary defects existing or both.

Table XI shows the distribution and the percentage distribution according to the type of house in District A and Ward 18 of District B for houses occupied by tuberculous families, for all houses in the area, for the tuberculous cases, and for the estimated population.

The actual numbers of persons living in houses of different types were not available; these were estimated by multiplying the number of houses, according to rooms and type, by the average number of persons occupying houses of corresponding size in the areas. There was no obvious association between the incidence of pulmonary tuberculosis and the fitness or otherwise of a house, but in Ward 18 of District B the number of houses involved was small.

This question was explored further by dividing the houses of District A and of Ward 18 of District B into two groups:

(1) Satisfactory, when the houses were of standard type or were classed as Substandard "A" or "B" with three or more rooms;

(2) Unsatisfactory, when the houses were classed as Substandard "A" or "B" with only one or two rooms, or as unfit.

With such a grouping the percentage of satisfactory houses among those occupied by tuberculous families was found to be higher than the percentage satisfactory of all houses both in District A and in Ward 18 of District B (33·6 per cent. compared with 29·2 per cent., and 60·8 per cent. compared with 49·4 per cent. respectively). Thus the occurrence of pulmonary tuberculosis would appear to be independent of the fitness, or otherwise, of the house.

## Discussion

In Glasgow at the present time, for those wards of the city in which the incidence of pulmonary tuberculosis is less than for the city as a whole, there is a high correlation between ward case-rates and the average number of rooms per house, the average number of persons per room, and the percentage of the population living more than two persons per room; for those wards of the city with a high incidence of disease there is no significant correlation with these overcrowding indices. This finding, taken in conjunction with the apparent absence of association with any particular aspect of individual housing in localized areas, suggests that in those wards of the city where the incidence of disease is high, factors must be operative which overshadow housing conditions in importance.

The larger size of the average tuberculous household, the association of tuberculosis with population density, and, in those wards of the city with high prevalence, the operation of factors other than housing will help to reconcile the somewhat conflicting views that have been expressed as to the role of housing in tuberculosis.

If the influence of housing is largely the result of housing density, Glasgow may be faced with a serious problem in her housing development, for the multi-storey development considered necessary may tend with its high housing density to nullify the beneficial effect on the incidence of tuberculosis that may derive from rehousing.

## Summary

Notifications of pulmonary tuberculosis in Glasgow during 1951 and 1952 are examined in relation to housing conditions in the 37 wards of the city. A more detailed examination is made of notifications during 1951 in two districts of the city: one

Table XI

CLASSIFICATION OF HOUSES

| District | Classification | Houses Occupied by Tuberculous Families | | All Houses Surveyed | | Tuberculous Cases | | Estimated Population | |
|---|---|---|---|---|---|---|---|---|---|
| | | No. | Per Cent. | No. | Per Cent. | No. | Per Cent. | No. | Per Cent. |
| A | Standard | 17 | 11·4 | 1,721 | 9·9 | 19 | 12·2 | 7,435 | 12·2 |
| | Substandard "A" | 55 | 36·9 | 6,745 | 38·9 | 57 | 36·5 | 23,494 | 38·5 |
| | Substandard "B" | 58 | 38·9 | 6,695 | 38·6 | 60 | 38·5 | 23,215 | 38·1 |
| | Unfit | 19 | 12·8 | 2,182 | 12·6 | 20 | 12·8 | 6,844 | 11·2 |
| | Totals | 149 | 100·0 | 17,343 | 100·0 | 156 | 100·0 | 60,988 | 100·0 |
| Ward 18 of District B | Standard | 25 | 49·0 | 2,945 | 41·9 | 26 | 50·0 | 11,960 | 47·5 |
| | Substandard "A" | 17 | 33·3 | 3,302 | 47·0 | 17 | 32·7 | 10,724 | 42·6 |
| | Substandard "B" | 9 | 17·7 | 727 | 10·4 | 9 | 17·3 | 2,325 | 9·3 |
| | Unfit | — | — | 49 | 0·7 | — | — | 151 | 0·6 |
| | Totals | 51 | 100·0 | 7,023 | 100·0 | 52 | 100·0 | 25,160 | 100·0 |

(District A) with a high and the other (District B) with a low incidence of the disease.

(1) The ward incidence of the disease is significantly correlated with the number of rooms per house, the number of persons per room, and the percentage of the population living more than two persons per room, all of which are themselves highly correlated.

(2) The association between these overcrowding indices and ward incidence appears to be restricted to the 21 wards with case-rates less than the city rate; in the sixteen wards with case-rates greater than the city rate there is no significant correlation. In this latter group of wards, factors other than housing must be operative in influencing the case-rates.

(3) The mean number of persons per room for the 21 wards having case-rates less than the city rate was 1·17 (standard deviation 0·289) and the mean for the sixteen wards with case-rates higher than the city rate was 1·49 (standard deviation 0·226).

(4) In both District A and District B the average tuberculous household was found to be larger than the average in the area. It is suggested that this may be explained in terms of the high incidence of disease in the adolescent and young adult age group, Families with adolescent and young adult members are usually approaching their maximum size, and this must result in a greater degree of overcrowding in tuberculous families, especially in houses of one and two rooms.

(5) In District A, no association between the incidence of pulmonary tuberculosis with overcrowding was apparent, but the tuberculous household was larger than the average household in the area.

(6) In District B, on the other hand, there was an association between the incidence of pulmonary tuberculosis and overcrowding. However, the percentage of tuberculous households living in one and two rooms corresponded closely with the percentage of all households in the district living in one and two rooms (64·0 per cent. and 63·0 per cent. respectively), and no association was found with either the number of rooms in the tuberculous house or the number of rooms occupied by the tuberculous household. It would seem, therefore, that this association is merely the reflection of the larger size of the tuberculous household.

(7) When contact cases were investigated, no association with overcrowding was established, though the numbers were small and any conclusion must be reserved.

(8) No association was found between the incidence of pulmonary tuberculosis and the fitness or otherwise of a house for human habitation.

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# OBSERVATIONS ON ROUTINE MEDICAL EXAMINATIONS OF UNIVERSITY ENTRANTS IN NORTHERN IRELAND

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## INTRODUCTION

The first complete academic year of the present student health service at the Queen's University of Belfast was 1949–50. Since that year every undergraduate entrant has been medically examined during his or her first year. At the end of each academic year the medical officer makes a formal report to a University sub-committee and includes statistical information about these routine examinations. This information is mainly limited to the detection and treatment of defects. In this paper we report other aspects of the 2,716 examinations carried out during the first 5 years of the service.

The data relate to age, sex, weight, height, sitting height, chest girth, chest expansion, pulse rate, systolic and diastolic blood pressures, vital capacity, visual acuity, colour vision, and hearing. All but ten of the 2,716 students were examined by the same physician (W.J.), assisted throughout by the same nursing sister, following the procedure and methods of measurement and assessment described in the next section. In subsequent sections, averages and standard deviations of quantitative measurements and distributions of qualitative assessments are analysed, with particular reference to age and sex variations. Some comparisons are made with other contemporary data, but these are few because of the variety of methods and criteria in published work.

In this report the word "significant" describes an estimate which, in relation to its standard error, is so large as to be unlikely to occur by chance more than once in twenty trials, *i.e.* $P < 0{\cdot}05$. Where standard errors are quoted, they follow the "$\pm$" sign after the estimate to which they refer. It has been convenient to use the analysis of variance technique in many instances and this analysis is given in the Appendix.

## EXAMINATION PROCEDURE AND METHODS

Each student attends for examination by appointment. On arrival the student is interviewed by the sister who starts an examination record. Men then undress, except for trousers, and women remove all outer garments; no shoes are worn. The sister measures weight, height, sitting height, and vital capacity, and tests visual acuity, colour vision, and hearing. The medical officer then makes a clinical examination: this includes measurement of chest girth and chest expansion and concludes with estimation of pulse rate and blood pressure. The sister's work usually takes about 20 to 30 minutes and the physician's about 40 to 60 minutes; thus the blood pressures are normally taken when the student has had at least one hour in the surgery.

The details of methods of measurement and assessment are as follows:

*Weight.*—Men wear trousers only and women are partially clothed; no shoes are worn. Measurement is made, to the nearest lb., on an Avery beam type machine with loose weights and a sliding scale; the apparatus is checked annually. Weights have been converted to kg.

*Height.*—No shoes are worn. Measurement is made, to the nearest cm., with a sliding horizontal cursor on a vertical scale. Students stand as erect as possible with feet together, looking straight ahead at eye level.

*Sitting Height.*—Measurement is made, to the nearest cm., with a sliding horizontal cursor on a vertical scale, which is fixed to the back of a small metal chair with a level seat. Students sit as erect as possible, looking straight ahead at eye level.

*Chest Girth.*—The chest is uncovered and measurement is made, to the nearest cm., with a tailor's measuring tape. The upper edge of the tape is put at the level of the fourth costo-chondral joint and the lower edges of

the scapulae, while the student stands erect with chest relaxed.

*Chest Expansion.*—Two further chest girth measurements are made as before except that, for one, the chest is fully inspired, and for the other, fully expired. Chest expansion is calculated as the difference, to the nearest cm., between these measurements.

*Pulse Rate.*—This is estimated in beats per minute. Beats are counted for 60 seconds timed with the second hand of a watch. Students lie on their backs on a couch.

*Blood Pressure.*—Systolic and diastolic pressures are measured, to the nearest 5 mm. Hg, with a Riva Rocci syphgmomanometer, which is periodically checked. Students remain on the couch after pulse rate is taken and are in this position for at least ten minutes before blood pressures are measured; by then they have been in the surgery for at least one hour. Systolic pressure is recorded at the instant when sounds are first heard and diastolic at the instant when sounds abruptly diminish prior to disappearance. The method conforms to the standards of the Cardiac Society of Great Britain and Ireland and the American Heart Association (1939).

*Vital Capacity.*—Measurement is made, to the nearest 0·1 litres, with a Kendrick vital capacity spirometer. The sister gives a demonstration to each student. Students have one "trial run" and the average of the next three attempts is the vital capacity recorded.

*Visual Acuity.*—Unaided visual acuity is tested, for each eye separately, using the standard Snellen type and illumination. Each eye is classified as 6/6, 6/9, 6/12, 6/18, 6/24, 6/36, or 6/60. (The limitations of this test are obvious and it is used to detect gross errors and as an indication of the need for more detailed examination.)

*Colour Vision.*—This is tested by the Ishihara (1943) method with pseudo-isochromatic plates, but no special illumination is used. Each student is classified as "normal" or "abnormal".

*Hearing.*—Each ear is tested separately, the untested ear being plugged with cotton wool. The sister, after expiration, whispers at a distance of 20 ft. from the student. If the whisper can be heard by each ear, hearing is classified as "normal"; if not, the defect is noted. If any diminution is detected, careful examination of the ear is made by the physician. If temporary causes, such as the presence of cerumen or upper respiratory infection, are observed, appropriate treatment is given and hearing retested after cure and the original results amended as appropriate. Thus in this analysis only permanent abnormality is noted.

## Age and Sex Distribution

More than 80 per cent. of the 2,716 students examined were aged 17–19 years, and although there were no significant differences in mean age of entrants between the five academic years (Appendix Serials 1 and 2), the high $\chi^2$ values of Table I suggest some such differences in age distribution. These differences were mainly due to the residual intake of ex-service students aged 20 and over in 1949–50, coupled with correspondingly fewer entrants in the youngest age group. The mean age of entry of men (19·3 yrs) was significantly higher than that of women (18·6 yrs) (Appendix Serial 3). Only 10·9 per cent. of the women, compared with 20·5 per cent. of the men, were aged 20 and over (Table I).

TABLE I

AGE AND SEX DISTRIBUTION OF ENTRANTS EXAMINED, BY YEAR OF ENTRY

| Sex | Year of Entry | Age Group (yrs) | | | | | Age (yrs) | |
|---|---|---|---|---|---|---|---|---|
| | | 17– | 18– | 19– | 20+ | Total | Mean | Standard Deviation |
| Male | 1949–50 | 51 | 174 | 85 | 114 | 424 | 19·8 | 3·9 |
| | 1950–51 | 78 | 162 | 72 | 77 | 389 | 19·1 | 3·3 |
| | 1951–52 | 75 | 173 | 89 | 87 | 424 | 19·3 | 3·5 |
| | 1952–53 | 62 | 182 | 73 | 71 | 388 | 19·2 | 3·5 |
| | 1953–54 | 45 | 172 | 69 | 55 | 341 | 19·2 | 3·7 |
| | Total | 311 (15·8) | 863 (43·9) | 388 (19·7) | 404 (20·5) | 1,966 (100) | 19·3 | 3·6 |
| Female | 1949–50 | 18 | 59 | 36 | 21 | 134 | 18·7 | 1·8 |
| | 1950–51 | 29 | 78 | 22 | 22 | 151 | 18·7 | 2·8 |
| | 1951–52 | 41 | 79 | 29 | 10 | 159 | 18·3 | 1·9 |
| | 1952–53 | 33 | 72 | 21 | 16 | 142 | 18·7 | 3·3 |
| | 1953–54 | 35 | 96 | 20 | 13 | 164 | 18·4 | 2·5 |
| | Total | 156 (20·8) | 384 (51·2) | 128 (17·1) | 82 (10·9) | 750 (100) | 18·6 | 2·5 |

Figures in brackets give percentage age distribution for each sex.

Comparison of age distributions between years of entry:
(*a*) Males, $\chi^2 = 30{\cdot}43$; $DF = 12$; $0{\cdot}01 > P > 0{\cdot}001$
(*b*) Females, $\chi^2 = 29{\cdot}18$; $DF = 12$; $0{\cdot}01 > P > 0{\cdot}001$.

TABLE II
PHYSICAL MEASUREMENTS

| Measurement | Sex | Mean Measurement for Stated Age Group (yrs) | | | | | Standard Deviation within Age Groups |
|---|---|---|---|---|---|---|---|
| | | 17– | 18– | 19– | 20+ | Total | |
| Weight (kg.) .. | Male M | 65·8 | 67·4 | 68·0 | 68·9 | 67·6 | 7·99 |
| | Female F | 57·9 | 58·6 | 58·9 | 58·8 | 58·6 | 7·46 |
| | Difference (M–F) | 7·9 ± 0·75 | 8·8 ± 0·47 | 9·1 ± 0·77 | 10·1 ± 0·91 | 9·0 ± 0·33 | |
| Height (cm.) .. | Male M | 172·0 | 172·1 | 171·7 | 170·4 | 171·6 | 6·06 |
| | Female F | 159·8 | 159·8 | 159·4 | 159·5 | 159·7 | 5·46 |
| | Difference (M–F) | 12·2 ± 0·56 | 12·3 ± 0·35 | 12·3 ± 0·57 | 10·9 ± 0·67 | 11·9 ± 0·24 | |
| Sitting Height (cm.) .. .. | Male M | 93·4 | 93·7 | 93·8 | 93·2 | 93·6 | 3·80 |
| | Female F | 88·6 | 89·0 | 89·0 | 88·6 | 88·8 | 3·59 |
| | Difference (M–F) | 4·8 ± 0·36 | 4·7 ± 0·22 | 4·8 ± 0·37 | 4·6 ± 0·44 | 4·8 ± 0·16 | |
| Chest Girth (cm.) | Male M | 88·4 | 89·4 | 90·0 | 90·5 | 89·6 | 4·94 |
| | Female F | 82·0 | 82·5 | 82·7 | 81·7 | 82·3 | 4·36 |
| | Difference (M–F) | 6·4 ± 0·45 | 6·9 ± 0·28 | 7·3 ± 0·46 | 8·8 ± 0·54 | 7·3 ± 0·19 | |
| Chest Expansion (cm.) | Male M | 8·0 | 8·1 | 8·1 | 7·8 | 8·0 | 1·33 |
| | Female F | 7·5 | 7·5 | 7·3 | 7·3 | 7·4 | 1·17 |
| | Difference (M–F) | 0·5 ± 0·12 | 0·6 ± 0·07 | 0·8 ± 0·12 | 0·5 ± 0·14 | 0·6 ± 0·05 | |

In what follows, the data are presented for each sex and age group separately, but for all five academic years combined. Thus mean measurements and qualitative distributions are based on the numbers in the total rows of Table I. The mean age of men in the oldest age group was 24·3 yrs; for women it was 23·5 yrs. Because of the heterogeneous nature of this age group, the examination of age variations of each measurement by analysis of variance has been supplemented by correlation coefficients between measurement and exact age.

## PHYSICAL MEASUREMENTS

*General.*—Table II gives the means of weight, height, sitting height, chest girth, and chest expansion. In each age group the means for men were significantly higher than those for women. Sitting height means were not significantly associated with age (Appendix Serials 8 and 9 and Table III). The means of each of the other four measurements of males differed significantly between age groups (Serials 4, 6, 10 and 12) and, although not significant (Serials 5, 7, 11, and 13), similar age trends occurred among females. These means (Table II) and the correlation coefficients (Table III) suggest, at least for males, that whilst weight and chest girth increased with increasing age even beyond age 20 years, height and chest expansion decreased. However, in all cases, the age effect was slight, and among males, on the assumption of a linear relationship, would amount to average differences, per increase of one year of age, of $+0·31 \pm 0·05$ kg. in weight, $+0·14 \pm 0·03$ cm. in chest girth, $-0·18 \pm 0·04$ cm. in height, and $-0·03 \pm 0·01$ cm. in chest expansion.

*Comparison with Other Series.*—Several reports on physical measurements of different population groups, some of which were composed of university students, have been made within the last 10 years. We have been able to obtain results in comparable age groups from the following:

(1) Bailey (1951) gave data on weight and height for about 3,000 Cambridge male freshmen aged 18–22 years for 1948–50. These men, representing about 75 per cent. of all freshmen, were volunteers. They were measured in trousers and without shoes.

(2) Grant and Hitchens (1953) reported weight data

TABLE III
CORRELATION COEFFICIENTS (*r*) BETWEEN AGE AND VARIOUS MEASUREMENTS

| Correlation between Age and Stated Measurement | All Students | | Students Aged 20+ yrs | |
|---|---|---|---|---|
| | Males | Females | Males | Females |
| Weight .. .. | 0·14** | 0·02 | 0·17** | −0·01 |
| Height .. .. | −0·06** | 0·03 | −0·09 | 0·14 |
| Sitting Height .. | −0·02 | 0·02 | 0·04 | 0·09 |
| Chest Girth .. .. | 0·10** | −0·03 | 0·19** | −0·05 |
| Chest Expansion .. | −0·08** | −0·08* | −0·10* | −0·15 |
| Pulse Rate .. .. | −0·08** | −0·06 | −0·11* | −0·12 |
| Systolic Blood Pressure .. .. | 0·03 | −0·04 | 0·10* | 0·08 |
| Diastolic Blood Pressure .. .. | 0·19** | 0·04 | 0·24** | 0·09 |
| Vital Capacity .. | −0·11** | −0·08* | −0·16** | −0·11 |

* $0·05 > P > 0·01$
** $P < 0·01$

for about 1,500 male and 800 female entrants, aged 17 years and over, to the University of Wales in 1949–51. These were also volunteers and again represented about 75 per cent. of all entrants. Men were measured in trousers, women were partially clothed, and none wore shoes.

(3) Kemsley (1951) reported extensive data on weight and height for about 27,500 men and 33,500 women, aged 14 years and over, in Great Britain in 1943. Details were given of the efforts made to obtain subjects in groups which would be reasonably descriptive of the general population. Although the subjects were clothed, adjustment to give nude weights were made before tabulation. To obtain results in our age groups we have interpolated linearly in Kemsley's Tables so that our references to his work are approximate.

(4) Martin (1949) reported data on weight, height, and chest girth for about 90,000 20-year old men of Great Britain who registered for military service during the pre-war months of 1939. These data are probably the most representative of any single age group of a large community yet published, although omissions include men in certain "reserved" occupations, those already in the armed services, and men so infirm that their medical examinations were not completed. All measurements were made without clothing or footwear and the chest was expanded for girth measurement.

(5) Clements and Pickett have given data on height, weight, and chest girth (Clements and Pickett, 1952, 1954a, 1954b) for about 3,700 men aged 18–42 years, who registered for military service in Scotland in 1941. All measurements were made with the subjects clad only in trousers, and reported chest girth was the mean of extreme inspired and expired chest girth measured with the upper edge of a tape touching the nipples and lower angles of the scapulae.

The possible comparisons between our results and those of these five series are shown in Table IV; where necessary, estimates have been converted to metric units and standard errors have been derived from published information. It will be appreciated that the comments which follow are of necessity limited to the age groups for which comparison is possible.

The present data, the Cambridge series of Bailey (1951), and the Welsh series of Grant and Hitchens (1953), are directly comparable in so far as methods of measurement are concerned. On the average, our men were significantly shorter than the Cambridge men by at least 5 cm., but the weights were about the same. Although the mean weights of our women were not significantly different from those of the Welsh University women, our men were significantly heavier by at least 1·9 kg.

The mean weights of our men and women were significantly greater than those reported for the "general population" groups by Kemsley (1951), Martin (1949), and Clements and Pickett (1952). But as the first two reported nude weights, it is reasonable to reduce the relevant differences in Table IV by about 1 kg. for men and about 2 kg. for women. After such correction, our means are still significantly higher, by some 5 to 9 kg. for men and by 5 kg. for women.

TABLE IV

COMPARISON OF PHYSICAL MEASUREMENTS WITH OTHER DATA

| Sex | Compared Data | | Age Group (yrs)* | Difference between Means (Present Data—Compared Data) | | |
|---|---|---|---|---|---|---|
| | Authors | Date | | Weight (kg.) | Height (cm.) | Chest Girth (cm.) |
| Male | Bailey | 1951 | 18–<br>19–<br>20+ | 0·0 ± 0·57<br>−1·0 ± 0·58<br>−0·9 ± 0·41 | −5·7 ± 0·55<br>−6·1 ± 0·40<br>−7·2 ± 0·36 | |
| | Grant and Hitchens | 1953 | 17– 18–<br>19–<br>20+ | 2·4 ± 0·40<br>2·1 ± 0·60<br>2·2 ± 0·55 | | |
| | Kemsley | 1951 | 17–<br>18–<br>19– | 10·5 ± 0·44<br>10·4 ± 0·36<br>9·3 ± 0·50 | 4·1 ± 0·40<br>3·2 ± 0·31<br>2·0 ± 0·42 | |
| | Martin | 1949** | 20–(*a*)<br>20–(*b*) | 6·4 ± 0·40<br>7·3 ± 0·44 | 0·3 ± 0·31<br>−1·0 ± 0·32 | −0·4 ± 0·26<br>0·1 ± 0·27 |
| | Clements and Pickett | 1952, 1954a, b | 17– 18– 19– | 6·2 ± 0·20 | 1·9 ± 0·25 | 2·5 ± 0·20 |
| Female | Grant and Hitchens | 1953 | 17– 18–<br>19–<br>20+ | 0·5 ± 0·48<br>0·7 ± 0·84<br>1·1 ± 1·17 | | |
| | Kemsley | 1951 | 17–<br>18–<br>19– | 6·4 ± 0·55<br>6·4 ± 0·42<br>6·3 ± 0·70 | 2·0 ± 0·42<br>1·7 ± 0·32<br>1·2 ± 0·47 | |

* Age x– years indicates age x years up to but not including age (x + 1) years.
** Compared with age group (*a*) 19– and (*b*) 20+ years of present series.

Our undergraduates were significantly taller, on average, than the subjects of comparable age and sex in the series reported by Kemsley (1951) and Clements and Pickett (1954a). The difference varied from about 1 to 4 cm. The mean chest girth of our men was also significantly greater than that reported by Clements and Pickett (1954b), but part of this might be attributed to different methods of measurement. Although it was impossible to make a direct comparison of comparable age groups with the series of Martin (1949), Table IV suggests that the means of height and chest girth of our series were very similar to those reported by him; as chest girth in his series relates to expanded chest it is reasonable to conclude that our men are in fact some 4 cm. bigger in average chest girth.

The incompleteness of Table IV and the lack of data at identical age groups makes any attempt to sum up these comparisons difficult. But for the heights of Martin's men, it would be reasonable to conclude that our men and women were taller and heavier, and that the men had a greater chest girth, on the average, than the general population groups at ages for which comparison could be made. On the other hand our men were shorter than those at Cambridge and heavier than those at the University of Wales.

## Clinical Measurements

*General.*—Table V gives estimates of mean pulse rate, systolic and diastolic blood pressure, and vital capacity. The relevant correlation coefficients are given in Table III.

*Pulse Rate.*—There were significant differences between the mean pulse rates of the four age groups (Appendix Serials 14 and 15), but for like age groups the sex differences were negligible (Table V). The age differences were largely due to low means in the oldest age group, although over the whole age range there was a small but significant negative correlation between age and pulse rate for men (Table III). The effect of this association was negligible; if linear regression is assumed, an average difference of $-0{\cdot}2 \pm 0{\cdot}05$ beats per minute per increase of one year in age might be expected.

For the male undergraduates at Cambridge, to which we have already referred, Bailey (1951) found a mean pulse rate of $70{\cdot}3 \pm 0{\cdot}3$ beats per minute, which is significantly, and quite considerably slower, than the mean in any age group of the present series. Bailey found no association with age and for all ages combined his mean was $8{\cdot}1 \pm 0{\cdot}4$ beats per minute slower than ours. His observations were also more widely dispersed than ours; the standard deviations were 11·4 and 8·7 beats per minute, a significant difference of $2{\cdot}7 \pm 0{\cdot}3$ beats per minute.

*Blood Pressure.*—The mean systolic pressure in men was significantly greater than that in women at each age group (Table V). Among males there were no significant differences in mean systolic pressure between ages. A low mean in the oldest age group was largely responsible for the female means not being similarly homogeneous (Appendix Serials 16 and 17), and the lack of significant correlation with age (Table III) among females supported this observation. It is of interest to note a small significant correlation of $r = 0{\cdot}10$ for males aged 20 and over, as this, coupled with the rather older mean age in this group of men than of women,

TABLE V
CLINICAL MEASUREMENTS

| Measurement | Sex | Mean Measurement for Stated Age Group (yrs) | | | | | Standard Deviation Within Age Groups |
|---|---|---|---|---|---|---|---|
| | | 17– | 18– | 19– | 20+ | Total | |
| Pulse Rate (beats per minute) .. .. | Male M | 78·5 | 78·8 | 78·8 | 77·2 | 78·4 | 8·69 |
| | Female F | 77·9 | 79·4 | 79·8 | 76·7 | 78·9 | 8·55 |
| | Difference (M–F) | $0{\cdot}6 \pm 0{\cdot}84$ | $-0{\cdot}6 \pm 0{\cdot}53$ | $-1{\cdot}0 \pm 0{\cdot}88$ | $0{\cdot}5 \pm 1{\cdot}04$ | $-0{\cdot}5 \pm 0{\cdot}37$ | |
| Systolic Blood Pressure (mm. Hg) .. .. | Male M | 129·3 | 130·0 | 130·6 | 129·9 | 130·0 | 10·87 |
| | Female F | 123·9 | 125·8 | 125·7 | 122·1 | 125·0 | 10·14 |
| | Difference (M–F) | $5{\cdot}4 \pm 1{\cdot}02$ | $4{\cdot}2 \pm 0{\cdot}64$ | $4{\cdot}9 \pm 1{\cdot}05$ | $7{\cdot}8 \pm 1{\cdot}24$ | $5{\cdot}0 \pm 0{\cdot}44$ | |
| Diastolic Blood Pressure (mm. Hg) .. .. | Male M | 70·1 | 70·9 | 71·2 | 73·7 | 71·4 | 8·24 |
| | Female F | 69·9 | 71·1 | 72·0 | 71·0 | 71·0 | 8·40 |
| | Difference (M–F) | $0{\cdot}2 \pm 0{\cdot}82$ | $-0{\cdot}2 \pm 0{\cdot}51$ | $-0{\cdot}8 \pm 0{\cdot}85$ | $2{\cdot}7 \pm 1{\cdot}01$ | $0{\cdot}4 \pm 0{\cdot}36$ | |
| Vital Capacity (litres of air) .. | Male M | 3·97 | 3·96 | 3·96 | 3·83 | 3·93 | 0·69 |
| | Female F | 2·72 | 2·73 | 2·71 | 2·59 | 2·71 | 0·55 |
| | Difference (M–F) | $1{\cdot}25 \pm 0{\cdot}06$ | $1{\cdot}23 \pm 0{\cdot}04$ | $1{\cdot}25 \pm 0{\cdot}06$ | $1{\cdot}24 \pm 0{\cdot}07$ | $1{\cdot}22 \pm 0{\cdot}02$ | |

might account for the sex difference in mean pressure being somewhat greater in that age group than in others.

Mean diastolic pressure in men increased significantly from the youngest to oldest age group but there were no significant differences between age groups of women (Appendix Serials 18 and 19). The correlation coefficients of Table III support these observations. Over the whole age range for males, $r = 0{\cdot}19$, and for the age group 20 and over, $r = 0{\cdot}24$. Between the two sexes the means were significantly different only in the oldest age group where the males had the higher mean pressure; this finding again might be partially due to the age association in males coupled with relatively more older men than women in that age group.

In the Cambridge series of male undergraduates Bailey (1951), no significant association of age with blood pressure was detected over the age range 18 to 22 years. His mean systolic pressure, $129{\cdot}7 \pm 0{\cdot}3$ mm. Hg, was not significantly different from that of our men, $130{\cdot}0 \pm 0{\cdot}25$, a difference of $0{\cdot}3 \pm 0{\cdot}39$ mm. Hg. His mean diastolic pressure, $79{\cdot}2 \pm 0{\cdot}2$ mm. Hg, however, was much higher than that found in any of our age groups. The difference between Bailey's mean and ours at all ages was $7{\cdot}8 \pm 0{\cdot}3$ mm. Hg, and that between Bailey's mean and our maximum in age group 20 years and over was $5{\cdot}5 \pm 0{\cdot}5$ mm. Hg.

Two recent genetical studies on arterial blood pressure have resulted in data being available for samples of the general population:

(1) Hamilton, Pickering, Roberts, and Sowry (1954) obtained arterial pressures from a sample of about 1,200 male and 800 female hospital out-patients aged 10 to 84 years. Patients were attending clinics where diseases affecting arterial pressure were unlikely to be seen.

(2) Miall and Oldham (1955) made measurements on a representative sample of the general population of a South Wales mining valley. The sample consisted of 137 males and 113 females aged 5 and over.

Both sets of workers used cubic equations to describe the relationships between pressure and age and, by substituting appropriate ages for each of our age groups in these equations, we have derived the "expected" average pressures shown in Table VI and compared these with our observed means.

The mean pressures for the South Wales sample were higher than the hospital sample at most age groups and Miall and Oldham felt that this was largely due to the methods of selection, although differences in arm circumferences and, possibly, in occupations, may also have had an influence. Nevertheless, at the ages for which comparison can be made, our systolic pressures were generally higher than both the South Wales and the hospital series. On the other hand, our diastolic pressures were very similar to the hospital series and consequently lower than the South Wales sample. It will be remembered that Bailey's means for the Cambridge men were similar to ours for systolic pressure; his diastolic means, however, more closely resemble those of South Wales.

Thus systolic pressures in both university series might be considered as unreasonably high. It might be argued, in many cases, that the strain of the young

TABLE VI

OBSERVED MEANS OF ARTERIAL PRESSURE (mm. Hg) COMPARED WITH THOSE EXPECTED FROM OTHER DATA

| Age (yrs) | Observed or Expected* | Mean Systolic Pressure | | Mean Diastolic Pressure | |
|---|---|---|---|---|---|
| | | Males | Females | Male | Females |
| 17·5 | Observed .. .. | 129·3 ± 0·62 | 123·9 ± 0·81 | 70·1 ± 0·47 | 69·9 ± 0·67 |
| | Expected (*a*) .. | 115·2 | 117·0 | 69·1 | 70·3 |
| | (*b*) .. | 121·5 | 115·3 | 77·9 | 73·6 |
| 18·5 | Observed .. .. | 130·0 ± 0·37 | 125·8 ± 0·52 | 70·9 ± 0·28 | 71·1 ± 0·43 |
| | Expected (*a*) .. | 115·3 | 117·1 | 69·5 | 70·6 |
| | (*b*) .. | 122·6 | 116·0 | 78·4 | 73·9 |
| 19·5 | Observed .. .. | 130·6 ± 0·55 | 125·7 ± 0·90 | 71·2 ± 0·42 | 72·0 ± 0·74 |
| | Expected (*a*) .. | 115·4 | 117·2 | 70·0 | 71·0 |
| | (*b*) .. | 123·5 | 116·8 | 78·9 | 74·3 |
| 23·5 | Observed .. .. | | 122·1 ± 1·12 | | 71·0 ± 0·93 |
| | Expected (*a*) .. | | 118·2 | | 72·6 |
| | (*b*) .. | | 119·8 | | 75·8 |
| 24·3 | Observed .. .. | 129·9 ± 0·54 | | 73·7 ± 0·41 | |
| | Expected (*a*) .. | 116·2 | | 71·9 | |
| | (*b*) .. | 127·3 | | 80·9 | |

* Expected (*a*) based on data of Hamilton and others (1954).
(*b*) based on data of Miall and Oldham (1955).

students' first rigorous medical examination tended to increase the pressure, even when care was taken to give reasonable resting time. Clearly more work is required in this field, in the shape of repeated estimates on the same students over a period of time. In this context it is of interest to note that when the blood pressures of 35 third-year male students were taken in 1956, as part of the pre-clinical examination given to all medical undergraduates, their systolic pressures were, in all but five cases, significantly lower than at their initial examination, 2 or 3 years earlier. The average decrease in systolic pressure was 5·9 mm. Hg ($t = 3{\cdot}38$; $DF = 34$; $0{\cdot}01 > P > 0{\cdot}001$). Corresponding diastolic pressures were very similar, the average difference being a negligible increase of 0·7 mm. Hg ($t = 0{\cdot}47$; $DF = 34$; $0{\cdot}70 > P > 0{\cdot}60$).

*Vital Capacity.*—The mean vital capacity of the men, but not of the women, was significantly different between age groups (Appendix Serials 20 and 21). Vital capacity decreased, on the average, as age advanced (Table V), and the correlation coefficients (Table III) suggest that this association with age became stronger after age 20. At each age group the means for males were significantly much greater by about 1·25 litres of air than those for females.

Whitfield, Waterhouse, and Arnott (1950) demonstrated the influence of various physical measurements on vital capacity and Garrad (1949) underlined the practical difficulties of comparing vital capacity estimates between different groups of individuals. Therefore no attempt is made here to compare the crude means with those of other workers.

## Vision and Hearing

*Visual Acuity.*—Table VII shows the percentage distribution of each sex, according to visual acuity.

TABLE VII
VISUAL ACUITY

| Visual Acuity | | Percentage Distribution | |
|---|---|---|---|
| | | Males | Females |
| 6/6 and Better | In both eyes | 59·46 | 58·40 |
| | In one eye, other worse | 12·51 | 11·87 |
| 6/9 or 6/12 | In both eyes | 6·26 | 5·73 |
| | In one eye, other worse | 5·65 | 4·80 |
| 6/18 to 6/36 | In both eyes | 5·24 | 4·53 |
| | In one eye, other worse | 3·00 | 4·53 |
| 6/60 or Less | In both eyes | 7·88 | 10·13 |
| Total | | 100·0 | 100·0 |

$\chi^2$ (on absolute numbers) = 8·74; $DF = 6$; $0{\cdot}2 > P > 0{\cdot}10$

Preliminary examination of similar distributions for the separate age groups showed no significant differences between age groups (for males $\chi^2 = 28{\cdot}55$; $DF = 18$; $0{\cdot}10 > P > 0{\cdot}05$, and for females, treating 19 years and over as one group, $\chi^2 = 15{\cdot}99$; $DF = 12$; $0{\cdot}20 > P > 0{\cdot}10$).

As Table VII shows, the sex differences were negligible, and just under 60 per cent. of the students had vision of 6/6 or better in both eyes. This proportion was somewhat below that found by Martin (1949) in his young adult males, and that reported by Bailey (1951) for the Cambridge male undergraduates. Table VIII compares the complete distributions from these two series with our male data; the high proportion of undergraduates of both universities with vision of 6/60 or less in both eyes is worth noting.

TABLE VIII
COMPARISON OF VISUAL ACUITY WITH OTHER DATA
(Males only)

| Visual Acuity | | Percentage Distributions | | |
|---|---|---|---|---|
| | | Present Data | Martin (1949) | Bailey (1951) |
| 6/6 and Better | In both eyes | 59·46 | 65·9 | 62·1 |
| | In one eye, other worse | 12·51 | 13·3 | 11·9 |
| 6/9 or 6/12 | In both eyes | 6·26 | 7·6 | 3·4 |
| | In one eye, other worse | 5·65 | 3·8 | 4·4 |
| 6/18 to 6/36 | In both eyes | 5·24 | 4·6 | 7·5 |
| | In one eye, other worse | 3·00 | 2·2 | 2·6 |
| 6/60 or Less | In both eyes | 7·88 | 2·6 | 8·1 |
| Total | | 100·0 | 100·0 | 100·0 |
| No. on which Percentages are Based | | 1,966 | 90,913 | 1,477 |

$\chi^2$ on absolute numbers:
Present data *v* Martin's data: $\chi^2 = 240{\cdot}92$; $DF = 6$; $P < 0{\cdot}001$
Present data *v* Bailey's data: $\chi^2 = 25{\cdot}24$; $DF = 6$; $P < 0{\cdot}001$

Sorsby, Benjamin, and Yudkin (1955) reported on the visual acuity of 501 men employed by the Post Office. In the age group 21 to 24 years, 68·6 per cent. had 6/6 or better vision in both eyes; this was again higher than our series, and although there was some slight selection of the postal workers due to minimum eye standards required on recruitment, it seems unlikely that it could account for the whole difference.

*Colour Vision.*—Of the 1,966 men examined, 136 (6·9 per cent.) were found to be colour blind. The 136 abnormal findings were varying degrees of red-green colour blindness. The importance of detecting such defects early in university life cannot

be over-emphasized. For some potential science students, the handicap is such that a change in their proposed course of study is often advisable.

A similar proportion (5·8 per cent.) was detected by Sorsby and others (1955) in their post-office workers (difference = 1·1 ± 1·2 per cent.), but Betenson (1955), in some 6,000 school medical inspections in Brecknock, found only 4·1 per cent. of the boys to be colour blind; this is significantly below our figure by 2·8 ± 0·6 per cent.

*Hearing.*—Table IX shows the proportions of students who had defective hearing. In all, this amounted to 7·17 per cent. of the men and 5·47 per cent. of the women. As the $\chi^2$ values show, age had no material influence upon this proportion among women, but it had among men, because in each age group up to age 20 years 6 per cent. were defective, while at age 20 and over the proportion was 11 per cent. Thus although in total the sex difference was unimportant (1·70 ± 1·01 per cent.), at age 20+ years it was significant and fairly large (6·26 ± 2·85 per cent.).

TABLE IX

HEARING

| Age Group (yrs) | Percentage with Defective Hearing | | Percentage Difference (Males—Females) ±Standard Error |
|---|---|---|---|
| | Males | Females | |
| 17– | 6·11 | 6·41 | −0·30 ± 2·39 |
| 18– | 6·03 | 4·95 | 1·08 ± 1·37 |
| 19– | 6·44 | 6·25 | 0·19 ± 2·48 |
| 20+ | 11·14 | 4·88 | 6·26 ± 2·85 |
| Total | 7·17 | 5·47 | 1·70 ± 1·01 |

On absolute numbers test for association with age:
Males $\chi^2 = 12{\cdot}09$; $DF = 3$; $0{\cdot}01 > P > 0{\cdot}001$
Females $\chi^2 = 0{\cdot}49$; $DF = 2$; $0{\cdot}80 > P > 0{\cdot}7$ (age groups 19– and 20+ combined).

## SUMMARY

(1) At the Queen's University of Belfast, in the 5 years 1949–54, 1,966 male and 750 female undergraduates were medically examined in their first year at the University.

(2) Average measurements are tabulated by age group and sex for weight, height, sitting height, chest girth, and chest expansion (Table II), and for pulse rate, systolic and diastolic blood pressure, and vital capacity (Table V).

(3) Distribution of the students by standard of visual acuity (Table VII) and hearing (Table IX) is also tabulated and colour vision is mentioned in the text.

(4) At the age range concerned, the male measurements of weight, height, chest girth, chest expansion, pulse rate, diastolic blood pressure, and vital capacity were all slightly associated with age; as age increased, weight, chest girth, and diastolic pressure increased while the others decreased. Above age 20 there was some indication of a small positive correlation between age and male systolic pressure.

(5) With the numbers available, few significant associations with age were observed in the female measurements. However, pulse rate and systolic blood pressure both tended to be significantly low at age 20 and over compared with younger women, and the correlations suggested a slight decrease in chest expansion and vital capacity with increasing age.

(6) On the average all the physical measurements, systolic pressure, and vital capacity were higher for men than for women of the same age.

(7) No sex or age differences were apparent in the distribution of the students by visual standards. Of all students about 60 per cent. had 6/6 or better vision in both eyes and about 8 per cent. had 6/60 or worse. Of the men about 7 per cent. were red-green colour blind.

(8) The percentage of men with defective hearing increased from just over 6 per cent. below age 20 to just over 11 per cent. above that age. This was not a feature of the tests on women, of whom 5·5 per cent. had defective hearing.

(9) The possible comparisons with other data are limited, but such comparisons do raise the question of the usefulness of including blood pressure readings in such examinations unless such readings are confirmed at follow-up examinations. Our systolic pressures were higher than those expected from the best standards at present available, but we have some evidence to suggest that part of this difference would have disappeared had the students been again examined at a later date.

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## APPENDIX TABLE

ANALYSIS OF VARIANCE

| Serial No. | Variable | Sex | Source of Variation | Sum of Squares | *DF* | Mean Square |
|---|---|---|---|---|---|---|
| 1 | Age (yrs) | Male | Between Yrs of Entry | 110·67 | 4 | 27·67 |
| | | | Within Yrs of Entry | 25,005·40 | 1,961 | 12·75 |
| | | | Total .. .. .. | 25,116·07 | 1,965 | |
| | | | $F = 2·17$; $n_1 = 4$, $n_2 = 1,961$; $0·10 > P > 0·05$ | | | |
| 2 | | Female | Between Yrs of Entry | 30·82 | 4 | 7·71 |
| | | | Within Yrs of Entry | 4,695·60 | 745 | 6·30 |
| | | | Total .. .. .. | 4,726·42 | 749 | |
| | | | $F = 1·22$; $n_1 = 4$, $n_2 = 745$; $P > 0·20$ | | | |
| 3 | | Both | Between Sexes .. | 325·45 | 1 | 325·45 |
| | | | Within Sexes .. | 29,842·49 | 2,714 | 10·97 |
| | | | Total .. .. .. | 30,167·94 | 2,715 | |
| | | | $F = 29·68$; $n_1 = 1$, $n_2 = 2,714$; $P < 0·001$ | | | |
| 4 | Weight (kg.) | Male | Between Age Groups | 1,750·05 | 3 | 583·35 |
| | | | Within Age Groups | 125,241·85 | 1,962 | 63·83 |
| | | | Total .. .. .. | 126,991·90 | 1,965 | |
| | | | $F = 9·14$; $n_1 = 3$, $n_2 = 1,962$; $P < 0·001$ | | | |
| 5 | | Female | Between Age Groups | 84·76 | 3 | 28·25 |
| | | | Within Age Groups | 41,531·68 | 746 | 55·67 |
| | | | Total .. .. .. | 41,616·44 | 749 | |
| | | | $F = 1·97$; $n_1 = 746$, $n_2 = 3$; $P > 0·20$ | | | |
| 6 | Height (cm.) | Male | Between Age Groups | 781·96 | 3 | 260·65 |
| | | | Within Age Groups | 71,968·23 | 1,962 | 36·68 |
| | | | Total .. .. .. | 72,750·19 | 1,965 | |
| | | | $F = 7·11$; $n_1 = 3$, $n_2 = 1,962$; $P < 0·001$ | | | |
| 7 | | Female | Between Age Groups | 16·78 | 3 | 5·59 |
| | | | Within Age Groups | 22,197·84 | 746 | 29·76 |
| | | | Total .. .. .. | 22,214·62 | 749 | |
| | | | $F = 5·32$; $n_1 = 746$, $n_2 = 3$; $0·10 > P > 0·05$ | | | |
| 8 | Sitting Height (cm.) | Male | Between Age Groups | 92·15 | 3 | 30·72 |
| | | | Within Age Groups | 28,285·05 | 1,962 | 14·42 |
| | | | Total .. .. .. | 28,377·20 | 1,965 | |
| | | | $F = 2·13$; $n_1 = 3$, $n_2 = 1,962$; $0·10 > P > 0·05$ | | | |
| 9 | | Female | Between Age Groups | 21·46 | 3 | 7·15 |
| | | | Within Age Groups | 9,601·29 | 746 | 12·87 |
| | | | Total .. .. .. | 9,622·75 | 749 | |
| | | | $F = 1·80$; $n_1 = 746$, $n_2 = 3$; $P > 0·20$ | | | |

| Serial No. | Variable | Sex | Source of Variation | Sum of Squares | *DF* | Mean Square |
|---|---|---|---|---|---|---|
| 10 | Chest Girth (cm.) | Male | Between Age Groups | 920·22 | 3 | 306·74 |
| | | | Within Age Groups | 47,851·97 | 1,962 | 24·39 |
| | | | Total .. .. .. | 48,772·19 | 1,965 | |
| | | | $F = 12·57$; $n_1 = 3$, $n_2 = 1,962$; $P < 0·001$ | | | |
| 11 | | Female | Between Age Groups | 71·61 | 3 | 23·87 |
| | | | Within Age Groups | 14,181·39 | 746 | 19·01 |
| | | | Total .. .. .. | 14,253·00 | 749 | |
| | | | $F = 1·26$; $n_1 = 3$, $n_2 = 746$; $P > 0·20$ | | | |
| 12 | Chest Expansion (cm.) | Male | Between Age Groups | 21·20 | 3 | 7·07 |
| | | | Within Age Groups | 3,500·51 | 1,962 | 1·78 |
| | | | Total .. .. .. | 3,521·71 | 1,965 | |
| | | | $F = 3·96$; $n_1 = 3$, $n_2 = 1,962$; $0·01 > P > 0·001$ | | | |
| 13 | | Female | Between Age Groups | 7·37 | 3 | 2·46 |
| | | | Within Age Groups | 1,018·21 | 746 | 1·36 |
| | | | Total .. .. .. | 1,025·58 | 749 | |
| | | | $F = 1·80$; $n_1 = 3$, $n_2 = 746$; $0·20 > P > 0·10$ | | | |
| 14 | Pulse Rate (beats per min.) | Male | Between Age Groups | 713·43 | 3 | 237·81 |
| | | | Within Age Groups | 148,161·04 | 1,962 | 75·52 |
| | | | Total .. .. .. | 148,874·47 | 1,965 | |
| | | | $F = 3·15$; $n_1 = 3$, $n_2 = 1,962$; $0·05 > P > 0·01$ | | | |
| 15 | | Female | Between Age Groups | 755·20 | 3 | 251·73 |
| | | | Within Age Groups | 54,498·67 | 746 | 73·05 |
| | | | Total .. .. .. | 55,253·87 | 749 | |
| | | | $F = 3·45$; $n_1 = 3$, $n_2 = 746$; $0·05 > P > 0·01$ | | | |
| 16 | Systolic Pressure (mm. Hg) | Male | Between Age Groups | 297·99 | 3 | 99·33 |
| | | | Within Age Groups | 231,651·96 | 1,962 | 118·07 |
| | | | Total .. .. .. | 231,949·95 | 1,965 | |
| | | | $F = 1·19$; $n_1 = 1,962$, $n_2 = 3$; $P > 0·20$ | | | |
| 17 | | Female | Between Age Groups | 1,176·77 | 3 | 392·26 |
| | | | Within Age Groups | 76,673·10 | 746 | 102·78 |
| | | | Total .. .. .. | 77,849·87 | 749 | |
| | | | $F = 3·82$; $n_1 = 3$, $n_2 = 746$; $0·05 > P > 0·01$ | | | |
| 18 | Diastolic Pressure (mm. Hg) | Male | Between Age Groups | 2,996·53 | 3 | 998·84 |
| | | | Within Age Groups | 133,151·45 | 1,962 | 67·87 |
| | | | Total .. .. .. | 136,147·98 | 1,965 | |
| | | | $F = 14·72$; $n_1 = 3$, $n_2 = 1,962$; $P < 0·001$ | | | |
| 19 | | Female | Between Age Groups | 325·00 | 3 | 108·33 |
| | | | Within Age Groups | 52,599·17 | 746 | 70·51 |
| | | | Total .. .. .. | 52,924·17 | 749 | |
| | | | $F = 1·54$; $n_1 = 3$, $n_2 = 746$; $P > 0·20$ | | | |
| 20 | Vital Capacity (litres of air) | Male | Between Age Groups | 5·37 | 3 | 1·80 |
| | | | Within Age Groups | 934·13 | 1,962 | 0·48 |
| | | | Total .. .. .. | 939·50 | 1,965 | |
| | | | $F = 3·78$; $n_1 = 3$, $n_2 = 1,962$; $0·05 > P > 0·01$ | | | |
| 21 | | Female | Between Age Groups | 1·21 | 3 | 0·40 |
| | | | Within Age Groups | 220·42 | 746 | 0·30 |
| | | | Total .. .. .. | 221·63 | 749 | |
| | | | $F = 1·37$; $n_1 = 3$, $n_2 = 746$; $P > 0·20$ | | | |

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# A NOTE ON THE ASSOCIATION BETWEEN SMOKING AND DISEASE IN MEN IN THE SEVENTH DECADE

BY

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The effect of smoking on disease has usually been assessed by comparing the smoking habits of persons with a specific disease with those of individuals believed to be representative of the general population of the same age and sex. This method has been criticized on various grounds, some of which are not very serious. Nevertheless it is admittedly difficult to assemble a control group which can be said with confidence to be wholly representative of the related population. The problem arises because there is no means of identifying the segment of the general population from which the affected individuals are drawn.

An alternative procedure which overcomes this and some other difficulties is an examination of smoking habits and disease incidence in a representative sample of the general population. This method has the merit that, if smoking is found to be associated with some diseases but not with others in the same population, one can have considerable confidence in the result. It has the disadvantage that a large sample is needed to give reasonable numbers of persons with any single disease. Investigations on these lines are those by Doll and Hill (1956) on approximately 40,000 registered medical practitioners in the United Kingdom, and by the Statistical Research Branch of the American Cancer Society on 188,000 men between the ages of 50 and 70. In both of these inquiries a history of smoking has been recorded, and is being related to subsequent mortality. So far as we are aware there are no data which relate the morbidity experience of a random sample of the general population to their smoking habits.

During 1956 the medical condition of a group of representative men in the seventh decade was assessed for the purposes of another inquiry, and the opportunity was taken to record their smoking habits. Eleven Birmingham general practitioners attempted to interview and examine all men on their lists aged 60–69. There were 1,243 men, of whom 1,062 (85·4 per cent.) were examined, the remainder being either untraced (58), dead (21), or not examined for other reasons (102), usually because the individual was not at home at the time of the general practitioner's visits. Since doctors made a serious attempt to see all patients in their own homes or in their surgeries, we are satisfied that no significant bias has been introduced. It has been shown elsewhere (Brown, McKeown, and Whitfield, 1957a) that the age distribution of the men examined is approximately the same as that of the male population of Great Britain, as indicated by the one per cent. sample of the 1951 Census, and apart from a small deficiency in Class IV the distribution by social class is reasonably consistent with that of Birmingham men aged 15 and over. (The one per cent. sample unfortunately does not give the class distribution of Birmingham males aged 60–69.)

The method used in recording amounts smoked was that employed in other inquiries (Doll and Hill, 1950). A man was regarded as a smoker if at any time he had smoked one cigarette per day (or ½ oz. tobacco per week) for a year. Smokers were asked at what age they started, how much they were smoking at the time of the inquiry, or, if they had given up smoking, the age at which they stopped and the amount smoked immediately before.

The medical data are derived from a full medical examination of "life insurance" type, performed by the general practitioners. In most cases it included a chest radiograph, and, whenever necessary, appropriate specialist investigation. In the case of coronary disease, which was the subject of a separate inquiry, all men with a suggestive history were referred to a hospital outpatient clinic for full investigation by one of us. (A.G.W.W.)

TABLE I

INCIDENCE OF DISEASE RELATED TO SMOKING HABITS

| Disease | Per cent. of Men Affected among: | | | | | | | Number of Men Affected |
|---|---|---|---|---|---|---|---|---|
| | Non-smokers | Pipe Smokers | Pipe and Cigarette Smokers | Cigarette Smokers who have given up Smoking | Cigarette Smokers (number per day) | | | |
| | | | | | 1–9 | 10–19 | 20 and over | |
| Bronchitis | 16·5 | 14·6 | 13·6 | 21·6 | 27·1 | 30·6 | 34·1 | 253 |
| Defective Hearing | 17·6 | 18·0 | 16·0 | 25·9 | 22·6 | 23·2 | 22·5 | 227 |
| Hypertension | 23·1 | 15·7 | 28·4 | 17·3 | 14·3 | 14·0 | 12·3 | 175 |
| Coronary A.D. | 9·9 | 8·4 | 8·6 | 6·8 | 12·8 | 7·7 | 5·8 | 88 |
| Peptic Ulcer | 6·6 | 6·2 | 7·4 | 6·2 | 8·3 | 9·2 | 13·0 | 87 |
| Defective Vision | 9·9 | 10·1 | 7·4 | 6·8 | 9·0 | 7·7 | 5·8 | 85 |
| Hernia | 6·6 | 5·6 | 8·6 | 6·2 | 6·8 | 7·7 | 5·8 | 71 |
| Arthritis | 7·7 | 5·1 | 6·2 | 8·6 | 8·3 | 6·6 | 2·9 | 68 |
| Number of Men at Risk | 91 | 178 | 81 | 162 | 133 | 271 | 138 | 1,054 |

In examining the association between smoking habits and disease incidence, we are restricted to conditions which are both common and compatible with a reasonable period of survival. Unfortunately this excludes cancer of the lung and pulmonary tuberculosis, two of the diseases in which an association has been reported. Table I gives the incidence of the eight diseases most frequently encountered in the sample according to smoking habits. In three cases—bronchitis, defective hearing, and peptic ulcer—incidence is higher in smokers than in non-smokers. In one case—hypertension—incidence appears to be higher in non-smokers than in smokers. In the other four conditions—coronary disease, defective vision, hernia, and arthritis—there is no evidence of association between incidence and smoking habits. In view of the rather small numbers we shall examine the relationship more closely only in the three commonest conditions.

The most consistent results are those for chronic bronchitis, which also has the highest incidence. For pipe smokers and mixed smokers incidence is approximately the same as for non-smokers; for cigarette smokers it is considerably higher, and increases consistently with increasing amounts smoked. Since bronchitis is known to be relatively more common among individuals in unfavourable social and economic circumstances, it was thought of interest to attempt to assess the relative importance of smoking habits and social class, defined in the usual way according to occupation. Table II gives the incidence of chronic bronchitis in men who have never smoked cigarettes and in cigarette smokers in relation to social class (mixed smokers, and cigarette smokers who had given up smoking are excluded). Because of small numbers, Classes I and II are combined. Among men who have not smoked cigarettes, the incidence of bronchitis is apparently unrelated to social class, whereas among smokers it increases sharply (from 20 per cent. in Classes I and II to 45·1 per cent. in Class V).

The last column of Table II gives an index of relative risk of the disease in smokers and non-smokers for each social class. It suggests that in Classes I and II an individual increases his risk of the disease very little by smoking, whereas in Class V the risk is trebled. It seemed possible that this result might be explained in part by variation in the number of cigarettes smoked by smokers (for example by an increase in amounts smoked from Classes I and II to Class V).

The fact that the mean number of cigarettes smoked daily is approximately the same for all classes (Table II) suggests that the different effect of tobacco in different social classes is probably attributable to variation in response rather than in the amounts of tobacco smoked. When it is remembered that some other infective diseases affecting the respiratory tract (for example pneumonia) are also more common in less favourable social circumstances, it is scarcely surprising that there should be variation in the response to tobacco in respect of a disease such as bronchitis.

TABLE II

INCIDENCE OF BRONCHITIS RELATED TO CIGARETTE SMOKING

| Social Class | Men who have never smoked Cigarettes | | Men Smoking Cigarettes | | | Relative Risk $\frac{(b)}{(a)}$ |
|---|---|---|---|---|---|---|
| | Number | Per cent. with Bronchitis (*a*) | Number | Mean Number of Cigarettes per Day | Per cent. with Bronchitis (*b*) | |
| I and II | 56 | 16·1 | 70 | 14·5 | 20·0 | 1·24 |
| III | 141 | 15·6 | 333 | 13·1 | 28·2 | 1·81 |
| IV | 29 | 13·8 | 57 | 13·5 | 36·8 | 2·67 |
| V | 43 | 14·0 | 82 | 12·9 | 45·1 | 3·22 |
| Total | 269 | 15·2 | 542 | 13·3 | 30·6 | 2·01 |

In Table III the data related to defective hearing have been prepared in the same form as Table II. The influence of social class is less consistent than in the case of bronchitis. While the observations leave little doubt that the incidence of defective hearing is higher in smokers than in non-smokers, the relative risk does not appear to increase regularly as social circumstances deteriorate. Nevertheless it is considerably higher in Class V than in the other three groups. It should perhaps be added that hearing was assessed with the use of aids, if they were normally used, and it is possible that the class variation reflects the use and quality of aids as well as of ears. It is unlikely, however, to affect a comparison according to smoking habits within the same class.

TABLE III

INCIDENCE OF DEFECTIVE HEARING RELATED TO CIGARETTE SMOKING

| Social Class | Men who have never smoked Cigarettes | | Men Smoking Cigarettes | | Relative Risk $\frac{(b)}{(a)}$ |
|---|---|---|---|---|---|
| | Number | Per cent. with Defective Hearing (*a*) | Number | Per cent. with Defective Hearing (*b*) | |
| I and II | 56 | 8·9 | 70 | 10·0 | 1·12 |
| III | 141 | 20·6 | 333 | 23·1 | 1·12 |
| IV | 29 | 24·1 | 57 | 24·6 | 1·02 |
| V | 43 | 16·3 | 82 | 31·7 | 1·94 |
| Total | 269 | 17·8 | 542 | 22·9 | 1·29 |

Finally, Table IV gives the same data in respect of hypertension. For the purpose of this assessment a man was regarded as hypertensive if his diastolic or systolic pressure were above 100 or 200 mm. Hg respectively. Elsewhere (Brown, McKeown and Whitfield, 1957b) we have examined mean aterial pressures according to smoking habits, and the results were consistent with the conclusion referred to above: pressures were lower in smokers than in non-smokers. It was also noted that both systolic and diastolic pressures tend to rise as economic and social circumstances become progressively less favourable (*i.e.* from Class I to Class V). However, Table IV does not suggest that the association between hypertension and smoking is consistently related to social class.

TABLE IV

INCIDENCE OF HYPERTENSION RELATED TO CIGARETTE SMOKING

| Social Class | Men who have never smoked Cigarettes | | Men Smoking Cigarettes | | Relative Risk $\frac{(b)}{(a)}$ |
|---|---|---|---|---|---|
| | Number | Per cent. with Hypertension (*a*) | Number | Per cent. with Hypertension (*b*) | |
| I and II | 56 | 8·9 | 70 | 10·0 | 1·12 |
| III | 141 | 19·9 | 333 | 13·8 | 0·69 |
| IV | 29 | 24·1 | 57 | 8·8 | 0·37 |
| V | 43 | 20·9 | 82 | 20·7 | 0·99 |
| Total | 269 | 18·2 | 542 | 13·8 | 0·76 |

SUMMARY

Observations on a little over 1,000 representative men in the seventh decade have been used to examine the incidence of the eight most common diseases according to smoking habits. Chronic bronchitis, defective hearing, and peptic ulcer were more frequent in smokers than in non-smokers; hypertension was more frequent in non-smokers than in smokers; and the incidence of coronary disease, defective vision, hernia, and arthritis was not consistently related to smoking habits.

It is shown that the well-known association between the incidence of chronic bronchitis and social circumstances is manifested only among cigarette smokers, incidence in those not smoking cigarettes being approximately the same in all social classes.

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